CHROMATOGRAPHIC METHODS OF ANALYSIS—GAS CHROMATOGRAPHY

Isadore Kanfer
Roderick B. Walker
Michael F. Skinner
Rhodes University, Grahamstown, South Africa

INTRODUCTION

History

The word "chromatography" is derived from the Greek words "chroma" and "graphein," which mean "color" and "to write," respectively, or "color writing." The initial use of the term is attributed to Tswett (1), who separated colored bands of plant pigments on a chromatographic column that consisted of an adsorbant powder that was washed with a liquid solvent termed the mobile phase. Substitution of this liquid mobile phase by a gas constitutes the fundamentals of gas chromatography (GC), where the solute to be separated is vaporized and carried down the length of a tube that contains an immobile solid or liquid phase, i.e., the stationary phase. The gaseous mobile phase serves to move the solute vapors along the column at rates dependent on several factors, the most important of these being temperature.

The first reported use of a vapor as the mobile phase is attributed to Martin and Synge (2) in 1941. They used the principles of partition chromatography, whereas James and Martin, in 1952, described the first application of this method, gas–liquid chromatography (GLC), for the analysis of fatty acids and amines (3). Gas adsorption chromatography (GSC), on the other hand, involves the use of a solid stationary phase and separation is based on an adsorptive mechanism. This technique was first described in 1947 in a doctoral thesis by Prior (4), under the supervision of Professor Cremer, and subsequently in their 1951 publication (5).

It was not, however, until 1955–1956 that the first commercial gas chromatographs were built (6, 7). Rapid progress in instrumentation and increased use of GC followed with the introduction of novel detectors, such as the flame ionization detector (8, 9), development of the capillary column (10), and the introduction of temperature programming and microsyringes for sample injection (6).

Utility

The introduction of GC as an analytical technique has had a profound impact on both qualitative and quantitative analysis of organic compounds. Identification of compounds by GC can be accomplished by their retention times on the column as compared to known reference standards, by inference from sample treatment prior to chromatography (11), or by the concept of retention index (12). The latter method and tables of retention indices (13) with associated conditions have been reported (14). Although qualitative data and analytical techniques for identification of compounds are well-established (15, 16) and relative retention data for over 600 substances also have been published (17), the main utility of GC undoubtedly lies in its powerful combination of separation and quantitative capabilities. Use in quantitative analysis involves the implementation of two techniques being performed concurrently, i.e., separation of components and subsequent quantitative measurement.

The use of GC was first included in the United States Pharmacopoeia (USP) in the sixteenth edition (18) in 1960, and became an official method of the British Pharmacopoeia (BP) in 1968 (19). GC has found widespread use in pharmaceutical analysis by virtue of its applications to purity and control analysis of raw materials, content and quality assessment of dosage forms (including product stability), and in the quantitative measurement of drugs in biological fluids. The latter application is important for therapeutic drug monitoring, pharmacokinetic studies, and bioavailability assessments. In fact, in a survey on GC use (20), a major application of this technique was in the field of pharmaceuticals.

When this article was first written several years ago, it appeared that the advent and establishment of high-performance liquid chromatography (HPLC) in pharmaceutical analysis had somewhat diminished with the utilization of GC. However, new regulatory requirements for drug approvals by the Federal Drug Administration

(FDA) and other regulatory agencies around the world, more particularly with respect to the determination of organic volatile impurities (OVI's) as well as other impurities and related substances (20), has resulted in more extensive use being made of GC in modern compendia, such as the USP 24th edition (21) and the 1999 edition of the BP (22). Perusal of the current USP (21) indicates that many more GC applications have been introduced since the 22nd edition of the USP. New inclusions have been incorporated in the tables in this article. Similarly, the recent edition of the BP (22) also includes numerous new applications. A list of compounds in the BP (which includes the European Pharmacopoeia) that use GC is included separately as an Appendix.

GC remains the chromatographic method of choice for thermally stable volatile compounds and for drugs, which are difficult to measure by HPLC due to detector insufficiency and/or inadequate resolution by the HPLC technique. The use of capillary columns in GC makes the method particularly attractive for difficult multicomponent analysis since extremely high resolution can be readily attained.

Modus Operandi

As previously mentioned, GC is a two-phase system that consists primarily of a stationary (solid and/or liquid) and mobile (gas) phase. When a liquid stationary phase is used (GLC), the liquid is immobilized as a thin film supported on a finely divided, inert solid support usually consisting of siliceous earth, crushed firebrick, glass beads, or in some cases, the inner wall of a glass tube. In GSC, the stationary phase is an active adsorbent, such as alumina, silica gel, or carbon, which is tightly packed into a tube.

Separation of components takes place in this tube (chromatographic column) following the introduction of sample at the tube inlet, which is subsequently swept through the column, partitioning or being dynamically adsorbed (or both) between the stationary and mobile phases during transit. The degree and speed of separation of components is governed by several factors, such as temperature, gas flow rate, and the physicochemical properties of the individual components being separated, as well as those of the stationary and to a lesser extent, mobile phase. Obviously, therefore, molecules with greater affinity for the stationary phase will spend more time either adsorbed to or partitioned within that phase and thus take longer to emerge from the column.

On emerging at the outlet, each component passes into a detector system that produces a signal that can be related to the mass of the individual component being detected. This signal is usually amplified electronically and subsequently recorded on a chart-recorder, integrator, or captured by an online data system. The resulting response is in the form of a signal–time plot or chromatogram, and is subsequently evaluated for either qualitative or quantitative use.

THEORETICAL PRINCIPLES AND RATE THEORY

A general account of chromatographic theory was presented in volume 2 of Encyclopedia of Pharmaceutical Technology (23). Therefore, the following discussion will focus specifically on GC theory. The separation of the component of a mixture depends upon the column performance (efficacy) and the relative retention capability of the stationary phase (selectivity). The former determines the width of the peaks relative to the length of time a component spends in the column, while the latter determines the relative position of each emerging component (resolution).

When the sample is introduced into the column, usually in the form of a zone of vapor, it takes the form of a narrow band. During transit through the column, various factors influence the width of this band, which is continuously increased due to various dispersion processes. These include diffusion of the solute, resistance to mass transfer between and within phases, and the influence of flow irregularities and perturbations (24). A simple concept, the "theoretical plate," carried over from distillation processes, has been used to compare columns and account for the degree of dispersion that influences bandwidth. A chromatographic column may be considered to consist of numerous theoretical plates where the distribution of sample components between the stationary and mobile phase occurs. Hence, a measure of the efficiency of a GC column may be obtained by calculating the number of theoretical plates, N, in the column from:

$$N = 16\left(\frac{t}{w}\right)^2 \text{ OR } N = 5.54\left(\frac{t^2}{w_{1/2}}\right) \quad (1)$$

where t is the retention time of the substance, w is the width of the base of the peak obtained by extrapolation (tangential extension of the sides of the relevant peak) of the relevant peak to the baseline, and $w_{\frac{1}{2}}$ is the peak width at half height (Fig. 1).

The higher the value of N for a column, the more efficient it will be. Columns with high efficiency allow smaller samples to be injected into shorter columns at

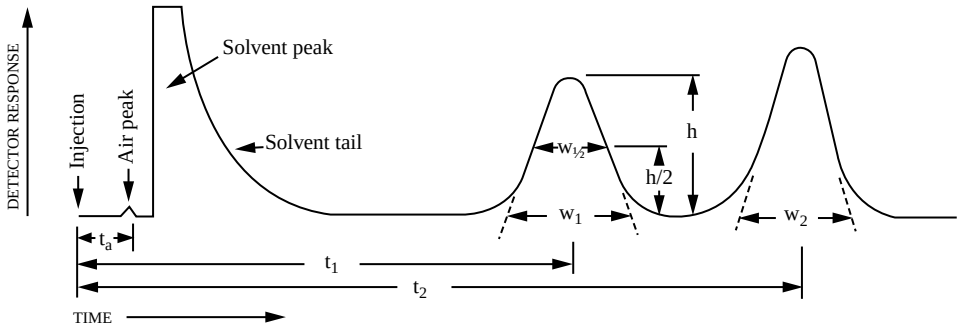

Fig. 1 Chromatographic separation of two substances.

lower temperatures, which results in high resolution of components in less time.

Column performance under different conditions or the comparison of different columns may be assessed by considering the height equivalent of a theoretical plate (HETP). Thus, HETP = *L*/*N* where *L* is the length of the column. Van Deemter et al. (25) derived an equation for dispersion in chromatography:

$$HETP = 2\lambda d_p + \frac{2\gamma D_g}{\mu} + \frac{8k^l d_f^2}{\prod^2 (1+k^l)^2 D_1}\mu \tag{2}$$

where λ is a constant related to the geometry of the column packing particles, d_p is the average diameter of the solid support particles, γ is a factor to correct for the "tortuosity" of the column's gas channels, D_g and $D1$ are solute diffusion coefficients in the gas and liquid phases respectively, d_f is the liquid film (stationary phase) thickness, k' is the partition coefficient of the solute, and μ is the linear gas velocity (26). Therefore, the Van Deemter equation expresses HETP as a function of the average mobile phase velocity μ and for a specific column, the equation has the general form:

$$HETP = A + \frac{B}{\mu} + C\mu \tag{3}$$

where *A* is the eddy diffusion term that results from flow inequalities in the column packing, *B* is the molecular diffusion term (when divided by μ it reflects axial diffusion in the mobile phase), and *C* reflects resistance to mass transfer from the stationary phase. The linear gas velocity, μ may be obtained from:

$$\mu = \frac{\text{Length of column}}{\text{Retention time of an unretained component (e.g., air)}} \tag{4}$$

The flow dependence of the three terms in the Van Deemter equation gives rise to a hyperbola (Fig. 2) when HETP is plotted against μ for a single component. The minimum is the flow rate at which the column will function at optimum efficiency. Fig. 2 also depicts how the *A*, *B*, and *C* terms contribute to the HETP. For maximum efficiency, these terms must be minimized, i.e., keep HETP as small as possible. Minimization of the A parameter is readily accomplished by using small uniform packing material particles in small diameter columns. Decreasing the particle diameter, d_p, lowers the HETP. However, below a certain particle size, flow of carrier gas through the column is restricted and results in pressure increases, which limits the reduction in particle size. Since λ is a measure of the column packing particle irregularities, the more uniform the size and shape of these particles, the smaller the value of λ.

The B parameter relates to the diffusivity of the solute in the carrier gas. Increases in molecular diffusion will result in increases in band broadening, which may, however, be controlled to some extent by increasing the

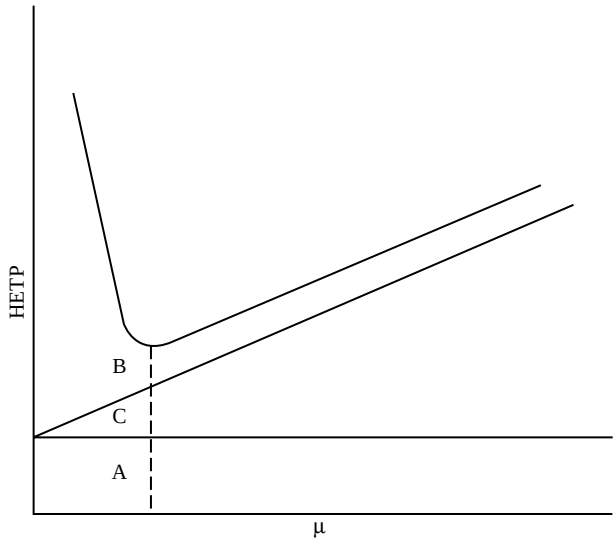

Fig. 2 Plot of HETP vs. flow velocity.

gas pressure. The use of a high-molecular-weight carrier gas will retard diffusivity and result in the best efficiency. However, detector function may be affected by the type of carrier gas used; hence, for the purposes of expediency, a compromise is often made by employing hydrogen or helium, which allows rapid analysis albeit with somewhat reduced efficiency. These aforementioned gases, which can rapidly diffuse into the stationary phase, are used at higher flow rates than nitrogen, another commonly used carrier gas.

The remaining parameter, *C,* is a measure of the mass transfer of the solute molecules from the stationary into the gas phase and depends upon several variables. These include the transfer of solute from liquid to gas and vice versa. Use of thin films of liquid phase will thus allow faster analysis at lower operating temperatures, although sample capacity will be reduced. Viscosity of the liquid stationary phase also affects mass transfer and therefore, should be kept as low as possible at the lowest possible temperature.

Golay (10) and Giddings (27), respectively, described a modification of the rate theory for capillary columns (hollow tube with inner wall coated with liquid phase) and the random walk, nonequilibrium theory. The former derived an equation to describe the efficiency of an open tubular column, while the random walk theory describes chromatographic separation in terms of statistical moments. The nonequilibrium theory involves a rigorous mathematical treatment to account for incomplete equilibrium between the two phases (28).

Selectivity is a function of the efficiency of the stationary phase with respect to its interactions with the solute vapor. Selection of an appropriate liquid stationary phase will even allow the separation of compounds that have the same vapor pressure. Separation is thus determined by the solubilities of the respective solutes in the stationary phase. Hence, the partition coefficient, k, is an extremely important parameter and is given by the following relationship:

$$k = \frac{\text{Concentration of solute in liquid phase}}{\text{Concentration of solute in gas phase}} \tag{5}$$

The efficiency of a stationary phase for a particular separation is measured by α, the relative retention, which is the ratio of two adjusted retention times (Fig. 1):

$$\alpha = \frac{t_2 - t_a}{t_1 - t_a} \tag{6}$$

where t_2 is the retention time of one of the components, t_1 is the retention time of a second or reference component in the mixture determined on the same column using the same separation conditions, and t_a is the retention time for an unretained compound, such as air. It is thus seen that α reflects the ratio of the partition coefficients for two components being separated under identical conditions and is a useful parameter for the identification of compounds when one of the components is a reference standard material (21). In order to express how well two peaks are actually separated, a resolution term, *R,* may be determined from Fig. 1, i.e.,

$$R = \frac{2(t_2 - t_1)}{W_2 + W_1} \tag{7}$$

where t_2 and t_1 are the retention times of the two components, and W_2 and W_1 are the corresponding widths of the bases of the peaks. Resolution is a measure of both column and stationary phase efficiency and relates peak width and maximal separation. In order to obtain complete separation (baseline resolution) between two peaks, the value of R must be a minimum of 1.5.

SYSTEM COMPONENTS/EQUIPMENT

Gases

While in principle any gas may be used in GC as the carrier, a prerequisite stipulates that the gas be inert with respect to both sample and stationary phase at the operating temperature. The carrier gas plays a critical role in the separation process and indeed, contributes to the efficiency of the system, as was shown in the Van Deemter equation where HETP depends on solute diffusivity in the gas phase. In practice, however, the importance of this role is relegated to a somewhat lower priority since the choice of carrier gas is usually dictated by the detector requirements. Helium is the gas of choice for use with the thermal conductivity detector (TCD), and allows greater sensitivity as compared to nitrogen. The electron capture detectors (ECD), on the other hand, are more efficient when nitrogen or argon–methane mixtures are used as carrier gas, while no noticeable difference in sensitivity is evident between nitrogen and helium when using the flame ionization detector (FID) (29). Thermionic detectors (TD), such as the nitrogen–phosphorus detector (NPD) utilize nitrogen or helium as the carrier gas. Similarly, the photoionization detector (PID) uses oxygen-free nitrogen or helium, while nitrogen is used as carrier gas with the flame photometric detector (FPD). All gases used as carriers in GC should be of high purity. A report on carrier gas purity in GC has been comprehensively discussed by Perretta (30), and procedures for the

preparation of "clean" gases were published previously (31). Traces of hydrocarbons can lower detector sensitivity (FID), trace amounts of water can desorb contaminants in the column, which leads to high background signals and/or "ghost peaks," while traces of oxygen can cause degradation of certain liquid phases, such as polyglycol and polyamides, which results in changes of solute retention times. Moisture can be removed by placing cartridges that contain an appropriate molecular sieve fitted in-line between the gas cylinder and the instrument. These type of filters also serve to remove other small, trace level contaminants, such as low-molecular weight hydrocarbons, and may be regenerated by heating with a slow flow of nitrogen for a few hours. Oxygen traps also should be used to protect stationary phases from oxidative degradation (32).

Flow Control

The carrier gas is fed into the GC via a pressure regulator, while flow controllers are used to control the mass flow rate. Maintenance of an accurate and constant carrier gas flow rate is essential for solute elution reproducibility in both qualitative and quantitative analysis. Normally, gas flow rates will decrease due to an increase in gas viscosity and column back pressure, with an increase in temperature, especially during temperature programmed work. Differential flow controllers are thus essential to assure a constant mass flow rate independent of the resistance of the column. In addition, detectors usually require gas flow control, and this can be accomplished using pressure regulators operating against flow restrictors. Gas flow rates can be simply measured at the end of the column with a soap bubble flow meter or by using rotometers. While flow control was previously adjusted manually, various manufacturers now offer software and associated hardware to effect such changes.

Sample Inlets

Various sample inlet systems have been designed with a primary objective of facilitating satisfactory vaporization of samples and subsequent transfer to the column as a compact "plug" in the shortest possible time and in an accurate and reproducible manner. Additional considerations for efficient sample introduction include maintenance of constant carrier gas flow rate and temperature during sample injection. Considerable differences, however, exist between the manner of sample injection and the actual injecting system, depending on whether packed columns or capillary columns are used. Therefore, sample volume considerations must be taken into account; whereas 1–10 μl is usual for packed columns, several orders of magnitude less is used with capillary columns. Inlet systems for packed columns usually consist of a heated injection block (Fig. 3) with a minimum dead volume port (to reduce band spreading) which is sealed with a special rubber septum through which the injection syringe needle may be inserted. Compounds which are thermally sensitive and unstable when in contact with metal surfaces may be protected by using glass liners that minimize the sample contact time with the metal injection block.

The foregoing discussion relates to the flash vaporization sample introduction technique that involves injection of sample into a precolumn zone that is kept at a temperature of 30–50°C higher than that of the column. This facilitates instantaneous sample vaporization. Samples also may be introduced by on-column injection where the sample is injected directly into the head of the column, which results in better precision than flash vaporization (33, 34).

Inlet systems for packed columns can often be used with capillary columns as well. However, the much smaller injection volumes and slower gas flow rates used with capillary columns, especially small-bore open tubular

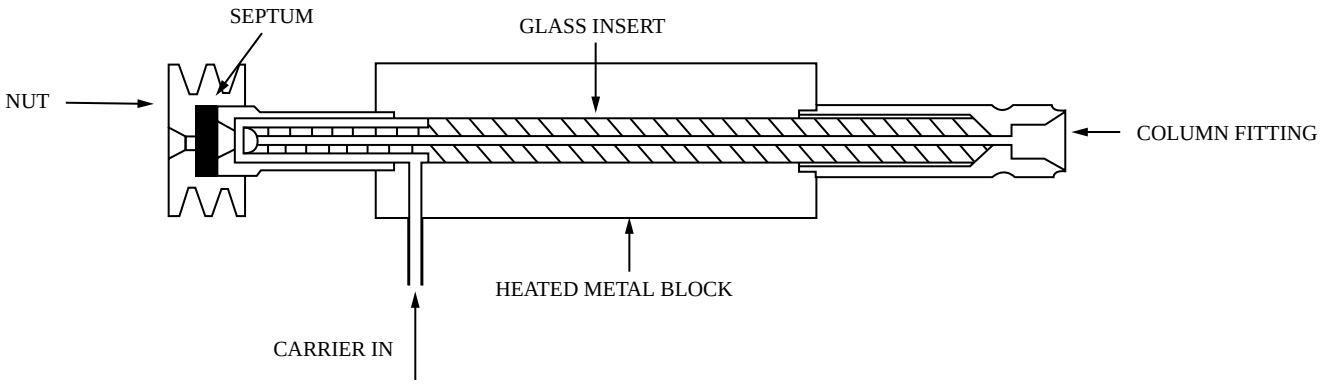

Fig. 3 Injection block.

capillaries (0.25 mm i.d.), require different sampling techniques.

Split injection

Early capillary inlets utilize an inlet splitter, which splits the sample into two unequal portions, the smaller of which goes into the column. The major function of the inlet splitter is not only to redirect the amount of sample placed on the column but also to permit rapid flushing of the injection chamber so that the sample in the column is followed by pure carrier gas, thereby avoiding sample dilution (35). The larger portion of sample is vented out of the system and the ratio of the two flows, the split ratio, typically ranges from 1:10 to 1:500. Since split injection is a flash vaporization technique, the possibility of sample discrimination exists. All sample components must be divided in the same ratio irrespective of differences in molecular weight, component concentration, polarity, injected volume, and inlet temperature for optimum reproducibility. Although the discriminatory effect can be minimized through the use of different inlet configurations (36), quantitative results by sample splitting are often not as good as by splitless and on-column techniques.

Splitless injection

Splitless injection utilizes a "solvent effect" (37) and allows a relatively large amount of dilute sample (1–5 μl) to be injected. The sample is vaporized and then carried onto the column on which it must be reconcentrated prior to analysis. This is essential in order to prevent band broadening. In order to prevent column overloading, the amounts of components being separated should be less than 50 ng. The large excess of solvent used to prepare the sample is backflushed 30–60 s after injection in order to minimize the occurrence of a long solvent tail, which can obscure any early eluting peaks. There are two mechanisms for reconcentrating the solutes at the head of the column. Grob and Grob (38) utilized the "solvent effect," whereby the solvent acts as a barrier to the sample components, which facilitates their condensation and concentration at the head of the column. This is due to the fact that when the sample components encounter a liquid phase mixed with retained solvent, the front of the sample plug undergoes stronger retention than the rear of the plug. In order to minimize column deterioration that can result from solvent overloading, a solvent in which the liquid phase is not readily soluble should be used. Both dichloromethane and hexane have been widely used and care should be taken to see that the initial column temperature is 10–30°C below the boiling point of the solvent selected.

Another method of reconcentrating the components at the head of the column is to keep the column temperature low enough to condense the solutes (cold trapping) (35). A general guideline for the use of this precolumn concentration technique is that compounds with boiling points 100°C higher than the column temperature will be cold trapped. Therefore, splitless injection should be used when component concentrations are too low for detection by split injection ($< 0.1\%$ sample) or when only a very limited amount of sample is available.

On-column injection

When dealing with thermolabile compounds, vaporization of the sample can result in degradation during this process. Schomburg et al. (39) described an on-column injection technique whereby the sample never encounters temperatures higher than the column temperature. This method also has been shown to be extremely useful for the separation of compounds that have low volatility and samples that have a wide boiling range. Using very fine long fused silica needles attached to a microsyringe and inserted into the capillary column bore, on-column systems have been described (40). The fine needles are too fragile for normal septum piercing, hence other methods have been devised in which a septum-free valved inlet is used (41).

Inlet modifications that incorporated air-cooling of the column inlet were later designed to overcome vaporization in the needle that resulted from the slow injections necessary to achieve a narrow band of injected sample (42).

Automatic injection

The injection process has been automated, thus facilitating batch processing of large numbers of samples that are completely unattended. Various automatic injector systems are commercially available for use with both packed and capillary columns. These are mainly based on the use of syringe injection and pneumatically operated under microprocessor control. Injector loops are largely used for the introduction of gases into the column, while manual injection continues to be extensively used. In the latter instance, the operator's injection technique can dramatically influence the quality of the analysis (35). A skilled operator may achieve precisions of the order of $\pm 1\%$ with manual syringes by careful debubbling of the syringe, and using sample sizes at least 50% of the syringe capacity to minimize needle hold up and setting errors, as well as using a very reproducible injection technique. However, the advent of automatic samplers considerably enhances injection precision and accuracy. In addition, the tedious process of carefully cleaning and flushing the syringe

between samples to avoid cross-contamination during manual injections is readily accomplished automatically.

Oven and Temperature Controls

The column is usually suspended in an insulated thermostatically controlled air oven through which the air is very rapidly circulated by means of fans or pumps. This allows accurate temperature control to within 0.1°C and minimizes thermal gradients. Provision is also made for the temperature to be rapidly increased and for the equally rapid cooling required with temperature-programmed work.

Injection port temperatures for packed columns include thermostatically controlled heating. These parts should be hot enough to rapidly vaporize the sample in order to prevent a loss in efficiency from the injection process. Heated detector systems also are used depending on the type of detector, to prevent sample condensation, which inevitably will result in peak broadening and loss of component peaks. Temperature control imparts stability to the detection system, often reducing noise and enhancing the detection limit. When the FID is used, its temperature must be kept high enough to avoid any water or by-products formed during the combustion process.

Detectors

A large variety of detectors have been designed for use in GC. In addition to numerous publications, several books and reviews that discuss the design and operating principles of GC detectors have been published (43–46).

The chromatographic detector, placed at the column exit, constantly monitors the emitted gas, and generates an electrical signal that is amplified and appears as a plot of detector response versus time, i.e., the chromatogram. Detectors may be "universal," which responds to every eluted component (TCD), "selective," which responds only to certain functional or elemental characteristics of the analyte (ECD and FID), or "specific," which provides qualitative information concerning the structure of the eluting component (FPD). However, for classification purposes, GC detectors generally fall into one of two groups: concentration-dependent and mass rate-dependent detectors. The former, which includes the TCD and ECD, produces a signal that is proportional to the concentration of the sample in the carrier gas. In the latter (e.g., FID), the detector signal is dependent on the mass of sample that flows through the detector per unit time (g/s). Some of the most important properties relating to detectors are: 1) their sensitivity, which is a function of the amount of component present in the injected sample; 2) their signal noise, which refers to random, short-term detector response and which combined with sensitivity, determines the detection limit for a given component; 3) their linearity of response, which indicates the region over which the detector signal is directly proportional to sample concentration or mass flow rate. The dynamic linear range of the detector is the range of sample size for which a signal is detected as a linear function of the sample size. Thus, a wide linear range is useful for quantitative analysis of multicomponent mixtures. In contrast to short-term noise, which depends upon electrical factors, temperature sensitivity, or flow variations, long-term noise is manifested by baseline drift in the chromatogram.

Detectors commonly used in GC and specified in the USP (21) include FID, alkali FID (NPD, TD), ECD, and TCD. A description of these detectors, including their operational principles and relative performance, was presented in a previous volume of this encyclopedia (23). Various other useful detectors for GC include photoionization (PID), flame photometric (FPD), electrolytic conductivity (ELCD), redox (RCD) and sulfur chemiluminescence (SCD), and helium ionization (HID) (47). Table 1 summarizes some of the features of detectors used in GC.

In addition to the above, several newer and highly sophisticated detection techniques that involve the coupling of various types of spectrometers with GC have emerged. These "hyphenated" techniques include the on-line interfacing of mass spectrometers (GC–MS) (57–60), infrared spectrometers that incorporate Fourier transformation techniques (FTIR–GC) (61), and FTIR–GC–MS (62). Generally, these are considered specific detectors mainly used to obtain qualitative information, although quantitative data can be obtained when operating a GC–MS system in the selected-ion-monitoring mode (SIM). This mode, in contrast to the normal scanning mode used for qualitative purposes, allows a single or a few characteristic ions of an analyte to be monitored and subsequently determined quantitatively (63, 64). Triple–quadruple MS/MS spectrometers are becoming more prevalent and these are being increasingly coupled to GC's that provide enhanced quantitation capabilities (60).

Columns

The suitability of a column for a particular use depends on various factors, such as stationary phase, solid support, column tubing material, inside diameter, percent liquid loading, and temperature. Columns may be prepared in

Table 1 Detector features

Detector	Classification	Response	Recommended carrier gas	Applications	Approximate detection capability (g)	Comments
TCD	Concentration	Universal	Hydrogen or Helium	Most compounds including water	10^{-6}–10^{-8}	Although less sensitive than other detectors, it is useful for moisture determinations (48), can detect some compounds unresponsive to FID and is non destructive and thus useful for preparative work
FID	Mass-flow	Universal	Argon, Helium or Nitrogen	Most compounds excluding water	10^{-10}–10^{-11}	Lack of response to water and carbon disulfide allows these to be used as solvents without interference with the analysis
ECD	Concentration	Selective	Hydrogen, Nitrogen or Argon/5–10% Methane	Compounds with high electron affinities, e.g. halogens	10^{-12}–10^{-14}	Good for electronegative compounds such as those containing extensively conjugated pi-electron systems, nitro- and highly conjugated aromatic compounds and compounds which can be readily derivatized to respond (49). Response depends also upon carrier gas flow rate
NPD	Mass-flow	Selective	Hydrogen, Helium or Nitrogen	Compounds containing nitrogen or phosphorus	10^{-12}–10^{-13}	Can be used in the flame or flameless mode. In the latter instance, a very low fuel (hydrogen) flow is used to form a plasma around a heated bead of potassium or rubidium salts. This results in a reduced response to hydrocarbons and subsequently less interference. Halogens as well as organolead compounds respond to the NPD detector in the flame mode. Phosphates (from cleaning detergents), chlorinated solvents and silanizing reagents can deplete the alkali beads and should thus be avoided (50)
PID	Concentration	Universal	Helium or Nitrogen	Compounds with ionization potentials $<$12eV	2×10^{-12}	Carrier gas must be free of oxygen and hydrocarbons to avoid a loss in sensitivity and interference, respectively. Water, sulfur dioxide, saturated hydrocarbons smaller than hexane, chloroform, methylene chloride, ethylene chloride and acetonitrile are not detected. The detector is non-destructive and can detect low levels of inorganic compounds. (51)

(Continued)

Table 1 Detector features (*Continued*)

Detector	Classification	Response	Recommended carrier gas	Applications	Approximate detection capability (g)	Comments
FPD	Mass-flow	Selective	Hydrogen or Nitrogen	Phosphorus and sulfur compounds	2×10^{-10}	Operated with a flame, photomultiplier tube and either a 393 or 526 nm bandpass filter for sulfur or phosphorus detection, respectively (52)
ELCD	Concentration	Selective	Helium or Nitrogen	Sulfur, nitrogen and halogen compounds	10^{-12}–10^{-13}	Following pyrolysis of column effluent, unwanted species are removed and the relevent products mixed with a liquid (alcohol/water) and differential conductivity subsequently measured. Depending upon the reaction gas used and whether the process is reductive or oxidative, specificity for nitrogen, sulfur or halogen compounds can be obtained (53)
RCD	Concentration	Selective	Helium	Compounds that react chemically to emit photons	2×10^{-11}	As with the ELCD, post-column treatment of the effluent is involved. The RCD responds to compounds that serve as reducing agents, such as alcohols, aldehydes, olefins, and carboxylic acids, and it is insensitive to many potentially interfering compounds such as water, oxygen, hydrocarbons and carbon dioxide (54)
SCD	Concentration	Specific	Helium	Compounds containing a sulfur—carbon bond	10^{11}–10^{-12}	Amenable sulfur compounds are reacted with fluorine to produce HF and the chemiluminescence is subsequently measured. Saturated hydrocarbons, methylene chloride, acetonitrile, methanol and carbon tetrachloride give little or no response (55)
HID	Mass-flow	Universal	Helium	Trace impurities in bulk gases and liquids	10^{-12}–10^{-14}	The helium carrier gas must be at least 99.9999% pure for optimum sensitivity. Useful to detect nitrogen oxides, sulfur gases, alcohols aldehydes, ketones, hydrocarbons and water (56)

various lengths and diameters depending on the particular objective. Preparative columns may range from 0.95 to 10 cm (3/8–4′) in diameter or larger for the collection of quantities of individual components when volumes between 0.5 ml and more are injected. Analytical (or packed) columns generally have outside diameters of 3, 4.7, or 6.25 mm (1/8, 3/16, or 1/4′), and inside diameters of 1–4 mm, while capillary columns with very narrow inside diameters are used for applications that require very high resolution. The inside diameter of the tubing is, in fact, one of the most critical column dimensions in determining the efficiency of separation.

Although packed GC columns may be made from various materials, such as glass, nickel, stainless steel, copper, aluminum, or even Teflon®, the USP (21) and BP (22) recommend that glass or stainless steel columns be used for pharmaceutical analyses unless otherwise specified. The advantage of using glass lies in its relative inertness as compared to metal columns, although its fragile nature is certainly a disadvantage. In order to assure further the inertness of glass, silanization of the inside walls with 5–10 vol% dimethyldichlorosilane in toluene is often performed (65).

Capillary columns are usually fabricated from fused silica, with a polyamide outer coating to impart flexibility and reduce breakage during handling. These columns can be classified into three categories according to the size of the internal diameter. Typical inside diameters are 0.53 mm, 0.32–0.22 mm, and 0.2–0.1 mm for megabore (wide-bore), normal bore (high-resolution), and microbore (high-speed), respectively.

The selection of a stationary phase is extremely important in GC since it is the major controllable variable of selectivity in the separation process. Stationary phases can be nonpolar, polar, or of intermediate polarity. Cyclodextrins, cyclic oligosaccharides composed of varying numbers of glucopyranose units, were found recently to be extremely useful for the separation of chiral compounds (66). Three types of derivatives, 5-hydroxypropyl (hydrophilic), dialkyl (hydrophobic), and trifluoroacetyl (intermediate) have been used, each of these phases having a selected area of specificity.

Capillary columns offer many advantages in terms of speed of analysis, high resolution, and overall very high separation efficiency. New applications that involve the use of capillary columns are included in the USP (21). In particular, methods for OVI analysis prescribe, almost exclusively, capillary columns, whereas approximately 20% of the other GC methods also prescribe such columns.

Solid supports should be chemically inert and exhibit a large surface area. Support materials used are diatomaceous earths, Teflon®, glass beads, and various polymers. Since the surface of the diatomaceous materials consist of silanol (Si—O—H) and siloxane (Si—O—Si) groups, compounds capable of hydrogen bonding (alcohols, acids, amines, etc.) can interact with these media, which results in tailing. This problem may, however, be minimized by silanization (65) following extensive acid washing to remove inorganic impurities. Acid-washed flux-calcined diatomaceous earth is often used for drug analysis.

Specially treated glass beads have been used as supports for high-molecular-weight compounds. The beads are usually etched and silanized prior to coating with the liquid phase. Teflon® is a useful support material for the analysis of short chain polar substances, which tail on diatomaceous supports, and is particularly indicated for the analysis of corrosive substances such as halogenated acids.

When a separation can be effected by a purely adsorptive mechanism (GSC), various adsorbants and porous polymers are used. Commercially available adsorbants include silica gel, activated charcoal, and molecular sieve materials. These adsorbants are used mainly for the analysis of gases and low-molecular-weight, low-boiling compounds (67).

Porous polymers also are useful for gas analyses and for very polar molecules, such as amines, glycols, and acids. Copolymers of styrene and divinylbenzene and others, such as ethylvinylbenzene–divinylbenzene, cross-linked acrylic ester, vinylpyridine, pyrollidone, and ethylene glycol dimethacrylate, are commercially available (29).

Open tubular columns are simply capillary tubes in which the inside of the column wall is used as the support for the liquid phase. These wall-coated open tubular columns (WCOT) have the stationary phase distributed in the form of a thin film on the inside surface of the open capillary tube, the walls thus serving as the support. In order to reduce the thickness of the liquid phase film, a porous layer may be formed on the inside wall of the capillary tubing and then coated with the liquid phase to produce a support-coated open tubular column (SCOT). Porous-layer open tubular columns (PLOT) are similar to SCOT columns, the difference being that in the former, the stationary phase is deposited on fine crystalline particles or glass powder which is adsorbed onto the walls of the tube. In both cases, the available surface area of the wall is increased, and allows an increased amount of liquid phase to be accommodated in the same length and diameter of tubing. The whisker-walled (WW) column consists of whiskers chemically etched on the surface of the wall, which also result in a significant increase in the available surface area. Wall-coated, porous-layer, and support-coated capillary columns are all available as whisker-walled, i.e., WWCOT, WWPLOT, and WWSCOT, respectively.

The stationary phase film thickness of capillary columns range from about 0.1–10 μm and can be divided into three film thickness ranges. Thin-film columns are usually 0.1–0.2 μm and offer the greatest stability. They have smaller sample capacity as compared to the thicker films but are the best for use with high temperatures. Thick films are usually 0.6–10 μm and allow higher sample loading, better retention for volatile compounds, and a high degree of inertness. Their main drawback, however, is larger bleed at high temperature as compared to the thin film type. The medium film thickness is about 0.3–0.6 μm and is a useful compromise in terms of sample capacity, retention properties, and phase stability.

In addition to the open tubular capillary columns, packed capillaries, and even micropacked capillaries, are commercially available. These columns contain support material, have internal diameters that range from 0.6–1.0 mm, and have the main advantage of being able to handle larger sample loadings. This is useful since direct analysis, as opposed to split-analysis, can be used with very short columns that operate at relatively high efficiency.

Column lengths of 0.3–6.1 m (1–20 ft) are commonly used and configurations can be straight, U-shaped, spiral, or flat coils. Straight and U-shaped columns are purported to be slightly more efficient than the coiled types. However, the dimensions of the GC oven usually dictate the choice. Capillary columns are generally much longer than packed columns and range in lengths from 10–100 m for the open tubular type and 1–6 m for packed type.

SEPARATION TECHNIQUES

Gas chromatographic analysis can be performed at constant temperature (isothermal mode) or with the column temperature increasing with time (temperature programming).

Isothermal

In isothermal GC, peak width increases linearly with retention time (68) and retention time increases exponentially with carbon number in a homologous series. In contrast, the peak width remains constant in programmed-temperature gas chromatography (PTGC) and retention times increase only linearly with carbon number in a homologous series (69).

Gas chromatographic methods for the analysis of impurities in pharmaceutical dosage forms and raw materials generally make use of isothermal techniques where the temperature of the instrument is maintained constant throughout the run. However, when complex mixtures that contain components with widely different boiling ranges need to be analyzed, PTGC is undoubtedly the method of choice. Separation of components in such a mixture may prove difficult if at all possible under isothermal conditions. Using a high temperature for the analysis may result in poor resolution between the rapidly eluting volatile components. On the other hand, operating at a lower temperature could cause excessively long retention times for the less volatile compounds, with resulting peak broadening leading to poor detectability and prolonged running times.

Temperature Programming

The advent in 1952 of PTGC (70) and the subsequent introduction of commercial equipment for temperature programming provided the necessary means to analyze complex mixtures that contained components of widely differing boiling points and solved some of the problems previously described in the section dealing with isothermal separations.

The PTGC technique involves increasing the column temperature at a preset rate during the elution process. This rate may be constant throughout the run, or periods of isothermal operation may be automatically programmed at set times between temperature increases. Generally, the electronically controlled ovens are designed to increase temperature at rates from 0.5–30°C per minute. The initial temperature should be chosen to minimize the retention time for the least retained solute, while the final temperature must be sufficient to elute the least volatile compound in a reasonable time. The instrument then automatically resets the temperature to the initial value in preparation for the next sample.

A major problem with PTGC, however, is that column bleed may cause baseline perturbations as the temperature increases, which results in interference with the analysis. Compensation for this effect is usually accomplished by using a dual column/dual detector system or replacing the liquid stationary phase with another less volatile coating. In the former instance, the output signal from the reference column is used to cancel out the bleed from the analytical column. Electronic compensation using single-column, single-detector systems are also available, as are GC's with electronically controlled programmed gas flows. In the latter case, the carrier flow rate is increased during the analysis, which results in reduced baseline drift by avoiding or reducing column bleed. Since lower temperatures can be used, the analysis of thermolabile

compounds is facilitated and a wider range of liquid phases can be used.

Special Techniques

Various compounds do not readily lend themselves to analysis by GC by virtue of several factors, such as nonvolatility, instability, elicitation of poor detector response, or high adsorptive properties (presence of polar groups). These problems sometimes can be overcome by the use of pyrolysis or by derivatization. The former technique involves high temperature decomposition of high-molecular-weight, nonvolatile substances to lighter, and more volatile compounds.

Derivatization is a valuable aid in GC. Suitable derivatives may be produced using synthetic organic reactions such as esterification, acylation, and silylation (29). These methods serve to increase thermal stability in unstable compounds, improve detectability in some instances (e.g., derivatives for electron capture detection) and often sensitivity, improve volatility in instances where the parent compound is relatively non-volatile, and mask polar groups to reduce adsorption. Several comprehensive reports and reviews on derivatization have been published over the years (71–74).

Quantitative and Qualitative Analysis

GC constitutes an analytical technique whereby the separation of components in a mixture and their quantitative and qualitative assessment can be performed simultaneously.

The area under the component elution peak is proportional to the concentration of that particular component. Various methods can be used to measure this area and are based on the assumption that the shape of the peak is Gaussian. Electronic integration is the preferred method since very accurate and precise measurements are obtained this way (RSD $\leq 0.5\%$).

Peak heights may be used but are less reliable since any variability in temperature and/or flow rate will affect this measurement. Peak areas may also be calculated by multiplication of the peak height and the width at half-height. This gives a value equal to 84% of the true area (75). Triangulation, planimetry, and cutting and weighing also can be used to measure peak areas.

In order to minimize the possibility of errors as a result of variable injection volumes, the internal standard (IS) method should be used. It involves the addition of a compound, the IS, which is not already present in the sample. This is normally a substance that elutes at a position near the sample component of interest and should be well resolved and readily detected under the given chromatographic conditions. The IS is added in constant amount to solutions that contain varying amounts of the analytical standard. Calibration curves are then constructed by plotting the ratio of either the areas or peak heights of the two peaks (analyte/IS) versus amount or concentration of analyte. The amount or concentration of each chromatographed sample can then be obtained by interpolation of the calibration curve. The calibration plot should be a straight line with an intercept of zero. However, nonlinear standard curves may result when the linear range of the particular detector is exceeded due to excess analyte concentration. The presence of high background and/or interfering compounds results in plots that have a positive intercept, while negative intercepts are usually indicative of sample loss during handling.

In contrast to the IS method, external standardization may be used in which several standard solutions of varying concentrations of the sample are prepared. Following constant volume injection of each standard solution, a plot of peak area (or height) versus concentration is made, and unknown sample concentrations are obtained from interpolation of the calibration curve. The success of this technique, however, is dependent upon the precision of injection volume, readily accomplished with automatic injection but less so when manual microliter syringes are used.

A further quantitative measure, normalization, is sometimes utilized to determine the proportion of one or more components in a mixture. This involves calculating the ratio of the individual component peak area to the sum of the areas of all component peaks in the chromatogram. It assumes that all the components have identical response factors to the detector. This is a reasonable assumption when all the components of the mixture are chemically similar. When structurally dissimilar components are analyzed, a response factor correction should be used by measuring the peak area for a known quantity of pure material and calculating the respective response factor (F) from:

$$F = \frac{\text{Component amount}}{\text{Peak area}} \tag{8}$$

Acquisition of qualitative data may be obtained by using specific detectors such as GC–MS, FTIR–GC, and FTIR–GC–MS, as well as from relative retention times or by the concept of retention index (vide infra).

Headspace Analysis

Specifications for pharmaceutical compounds, in addition to the actual active ingredient itself, include information and limits relating to the intermediates, residual solvents, and other volatile impurities (21) associated with their preparation.

Headspace analysis is a very effective technique for the analyses of volatile compounds, and is particularly valuable when direct injection would ruin the column due to corrosive or highly nonvolatile components present in the sample. Headspace analysis obviates extensive sample preparation, eliminates the possibility of unwanted component interference, and avoids degradation of susceptible components in the injection port or on the column (76).

The liquid or solid sample is placed in a vial, which is sealed with a septum and heated to a predetermined temperature for a period of time. Equilibrium between the sample and vapor phase is then established and a portion of the volatiles in the gas phase (headspace) is subsequently injected onto the column. Several different methods have been used to transfer headspace volatiles into the GC, from manual withdrawal that uses a gas syringe, to sophisticated automatic sampling that involves transfer lines, and valves that lead directly onto the column.

Two main techniques, however, may be used. These are static and dynamic sampling. The static method allows the temperature of the sample container to be held for a sufficiently long period to allow the gas-phase and sample-phase to equilibrate. The dynamic sampling uses an inert gas that is swept over or through the thermostated sample for a period of time sufficient to extract most or all of the volatile components. A general chapter on OVI's, in which five OVI's are specifically mentioned (chloroform, dichloromethane, benzene, trichloroethylene, and dioxane), was introduced into the USP (21). Previously, the USP included methods II and III, which provided an alternative to direct injection and specified dynamic headspace sampling. These, however, have now been excluded and method IV provides for the general use of static headspace sampling (77). Method VI, while still included, prescribes analysis by direct injection into a gas chromatograph, but none of the monographs in the USP or National Formulary (NF) specify use of method VI for OVI testing. The trend, it appears, has been toward using method IV as a replacement for other methods in individual monographs and that monographs that now specify method IV, originally specified method VI (78). The advantages, sampling techniques, and problems associated with headspace sampling were previously discussed by Hinshaw (79).

PHARMACEUTICAL APPLICATIONS

Applications of GC to the analysis of pharmaceuticals have been described in several books, compendia, and the review of Jack (80) to which the reader is referred. In addition, the reader might want to review the three-part multi-authored series (81) that includes HPLC determinations, as well as the comprehensive listing of published chromatographic methods in a book edited by Adamovics (82).

Although HPLC has largely superseded GC as the compendial chromatographic method of choice for the assay of pharmaceuticals, the application of GC continues to be an important and valuable analytical method for monitoring certain impurities and for the determination of various related substances and OVI's in many pharmaceutical dosage forms, as well as in raw materials. GC, furthermore, continue to be a valuable tool for the analysis of drugs in biological fluids for the purposes of therapeutic drug monitoring, pharmacokinetic studies, and in the assessment of bioavailability/bioequivalence.

A large number of pharmaceutical compounds can, however, be analyzed by either GC or HPLC. In terms of cost effectiveness, given that the equipment is available, GC often may be preferred due to its advantage of avoiding the use of expensive solvents and associated subsequent disposal problems.

Raw Materials (Bulk Drugs) and Dosage Forms

Both the USP/NF (21) and the BP (22) utilize GC for the following types of determinations:

1. Assay.
2. Chromatographic purity.
3. Identification.
4. Presence of volatile matter, intermediates, and related substances.
5. Water.
6. Presence of isomers, isomeric purity, and racemate ratios.
7. Alcohol content.

Tables 2–11 list the various compounds and the associated USP tests, together with their relevant chromatographic conditions. Drugs and related dosage forms have been arranged alphabetically, while descriptions of the various GC supports and liquid (coating) phases largely correspond to the abbreviations used in the USP. These are given starting on page 409:

Table 2 Compendial applications of GC for the assay of pharmaceutical raw materials and dosage forms

Material/dosage form	Column	Carrier gas	Temp. (°C)	Detector	Internal standard	Reference
Acetone	1.8 *M* × 3 mm I.D. S4	Helium	110–220 8/min	FID	None	NF (19, p. 2409)
Acetyltributyl Citrate	30 *M* × 0.32 mm I.D. Column Bonded with G42 (0.5μm)	Helium	80–220 20/min	FID	None	NF (19, p. 2409)
Amantadine Hydrochloride capsules Amantadine Hydrochloride syrup	Glass, 1.22 *M* × 2 mm I.D. 10% G1/S1A (100–120 mesh)	None Specified	115	FID	Naphthalene	USP (24, pp. 103 and 104)
Amitraz Amitraz concentrate for dip	1.5 *M* × 4 mm I.D. 3% G1/S1A	Nitrogen	250	FID	Squalane	USP (24, p. 121)
Amylene Hydrate	Glass, 2 *M* × 4 mm I.D. S2	Helium	190	TCD	None	NF (19, p. 2414)
Atropine Sulphate ophthalmic ointment	Glass, 1.8 *M* × 2 mm I.D. 3% G3 /S1AB	Nitrogen	225	FID	Homatropine	USP (24, p. 179)
Atropine Sulphate ophthalmic solution Atropine Sulphate tablets					Hydrobromide	USP (24, p. 179)
Avobenzene	Fused Silica 25 *M* × 0.32 mm Capillary coated with G1	Helium	200–280 4/min	FID	None	USP (24, p. 181)
Belladona extract	Glass, 1.2 *M* × 4 mm I.D. 3% G3/S1AB	Helium	215	FID	Homatropine	USP (24, pp. 199, 200 and 201)
Belladona extract tablets Belladona leaf Belladona tincture						
Benzocaine and Menthol topical aerosol	1.8 *M* × 2 mm I.D. 10% G16/S1AB (for Menthol)	Helium	170	FID	Decanol	USP (24, p. 208)
Benzyl Alcohol	Glass or Stainless Steel, 1.8 *M* × 3 mm I.D. 5% G16/S1	Helium or Nitrogen	140	FID	Phenol	USP (24, p. 1865)
Butabarbital	1.8 *M* × 4 mm I.D. 10% G37/S1AB		260	FID	Tetracosane	USP (24, p. 261)
Butabarbital Sodium elixir	Glass, 0.9 *M* × 4 mm I.D. 3% G10/S1A (80–100 mesh)	Nitrogen	200	FID	Secobarbital	USP (24, p. 262)
Butabarbital Sodium tablets						
Butane	Aluminum, 6 *M* × 3 mm I.D. 10% liquid G 30/S1C	Helium	33	TCD	None	NF (19, p. 2422)
Butylated Hydroxyanisole	Stainless Steel, 1.8 *M* × 2 mm I.D. 10% liquid G26/S1A	Helium	175–185	FID	4-tert-butylphenol	NF (19, p. 2422)
Castor Oil emulsion	Glass, 1.8 *M* × 4 mm I.D. G25/S1	Helium	245	FID	Di(2-ethylhexyl) pthalate	USP (24, p. 323)
Cetostearyl Alcohol	2 *M* × 3 mm I.D. 10% liquid G2/S1	Helium	205	FID	None	NF (19, p. 2434)

(Continued)

Table 2 Compendial applications of GC for the assay of pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage form	Column	Carrier gas	Temp. (°C)	Detector	Internal standard	Reference
Cetyl Alcohol	2 *M* × 3 mm I.D. 10% liquid G2/S1A	Helium	205	FID	None	NF (19, p. 2435)
Chlorobutanol	Glass or Stainless Steel, 1.2 *M* × 3 mm I.D. 5% G16/S1A	Helium or Nitrogen	110	FID	Benzaldehyde	USP 24, p. 1865
Chloroxylenol	Glass, 1.8 *M* × 4 mm I.D. 3% G16/S1A	Nitrogen	210	FID	None	USP (24, p. 391)
Clindamycin Palmitate Hydrochloride	Glass, 0.6 *M* × 3 mm I.D. 1% G36/S1AB (80–100 mesh)	Helium	290	FID	Cholesteryl Benzoate	USP (24, pp. 431 and 432)
Clindamycin Palmitate Hydrochloride fororal solution						
Clioquinol	Glass, 1.83 *M* × 2 mm I.D 3% G3/S1AB (80–100 mesh)	Helium	165	FID	Pyrene	USP (24, pp. 435 and 436)
Clioquinol cream						
Clioquinol ointment						
Clioquinol and Hydrocortisone cream						
Clioquinol and Hydrocortisone ointment						
Cyclomethicone	3.66 *M* × 3 mm I.D. 20% liquid G1/S1A (60–80 mesh)	Helium	125–320 8/min	TCD	None	NF (19, p. 2443)
Desflurane	Stainless Steel, 3.7 *M* × 2.4 mm I.D. 10% G31 and 15% G18/S1A	Helium	80–88 2/min 88–175 70/min	FID	Halothane	USP (24, p. 504)
Dibutyl Sebacate	1.8 *M* × 2 mm I.D. 10% liquid G41/S1A (100–120 mesh)	Helium	150–280 4/min	FID	None	NF (19, p. 2445)
Dichlorodi-fluoromethane	Stainless Steel, 1.8 *M* × 2 mm I.D. 1% G25/S12	Helium	70–170 10/min	FID	None	NF (19,pp. 2445 and 2446)
Dichlorotetrafluoroethane						
Dicyclomine Hydrochloride capsules	Fused Silica 15 *M* × 0.5 mm coated with G3 (1 μm)	Nitrogen	160° – 240°20°/min	FID	Phenacetin	USP (24, pp. 549, 550 and 551)
Dicyclomine Hydrochloride injection						
Dicyclomine Hydrochloride syrup						
Dicyclomine Hydrochloride tablets						
Dimethyl Glycol Monoethyl ether	30 *M* × 0.32 mm I.D. fused Silica column with G46(1 μm)	Helium	120–225 12/min	FID	None	NF (19, p. 2447)
Dimethyl Sulfoxide gel	1.8 *M* × 4 mm I.D. 15% G39/S1A	Helium	160	FID	Dimethyl-for-mamide	USP (24, p. 580)
Dimethyl Sulfoxide irrigation	Glass, 1.5 *M* × 3 mm I.D. 10% liquid phase G25 on packing S1A	Helium	100–170 10/min	FID	Dibenzyl	USP (24, p. 581)

(Continued)

Table 2 Compendial applications of GC for the assay of pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage form	Column	Carrier gas	Temp. (°C)	Detector	Internal standard	Reference
Dimethyl Sulfoxide topical solution	1.8 *M* × 4 mm I.D. 10% liquid phase G16 on packing S1A	Helium	170	FID	Dimethyl-formamide	USP (24, p. 581)
Diphenoxylate Hydrochloride and Atropine Sulfate oral solution	Glass, 1.2 *M* × 4 mm I.D. 3% G3/S1 (for Atropine Sulfate)	Helium	230	FID	Homatropine Hydrobromide	USP (24, p. 585)
Enflurane	Stainless Steel, 3 *M* × 4 mm I.D. 20% G4/S1A (60–80 mesh)	Helium	60–125 6/min	TCD	None	USP (24, p. 642)
Conjugated Estrogens Conjugated Estrogen tablets Esterified Estrogens Esterified Estrogen tablets	15 *M* × 0.25 mm I.D. fused Silica capillary bonded with G19 (0.25 μm)	Hydrogen	220	FID	3-O-Methylestrone	USP (24, pp. 681, 682, 683 and 684)
Ethchlorvynol	Glass (pre-treated with 10% dimethyldichlorosilane in toluene), 1.8 *M* × 4 mm I.D. 10% G16/S1AB (60–80 mesh)	Helium	160	TCD	None	USP (24, p. 691)
Ethclorvynol capsules	Glass (pre-treated with 10% dimethyldichlorosilane in toluene), 1.8 *M* × 4 mm I.D. 10% G16/S1AB (60-80 mesh)	Helium	160	FID	Chlorobutanol	USP (24, p. 691)
Eucalyptol	60 *M* × 0.32 mm I.D. Fused Silica capillary G16	Helium	60–200 6/min	FID	None	USP (24, p. 705)
Guaifenesin and Codeine Phosphate syrup	0.6 *M* × 2 mm I.D. 3% liquid G3/S1A (100–120 mesh) (For Codeine Phosphate)	Helium	210	FID	Hydrocodone Bitartrate	USP (24, p. 793)
Guaifenesin and Codeine Phosphate syrup	1.2 *M* × 4 mm I.D. 3% liquid G6/S1A (100–120 mesh) (For Guaifenesin)	Helium	170	FID	Dipropyl Phthalate	USP (24, p. 793)
Homosalate	30 *M* × 0.53 mm I.D. G27 (1 μm)	Hydrogen	70–220 6/min	FID	None	USP (24, p. 816)
Hydroxypropyl Methylcellulose	Glass, 1.8 *M* × 4 mm I.D. 20% G28/S1C (100–120 mesh)	Helium	130	TCD	Toluene	USP (24, p. 843)
Hyoscyamine tablets	Glass, 1.8 *M* × 2 mm I.D. 3% liquid G3/S1AB	Nitrogen	225	FID	Homatropine Hydrobromide	USP (24, p. 850)
Hyoscyamine Sulphate elixir Hyoscyamine Sulfate injection Hyoscyamine Sulphate oral solution Hyoscyamine Sulphate tablets	Glass, 1.8 *M* × 2 mm I.D. 3% liquid G3/S1AB	Nitrogen	225	FID	Hydrobromide	USP (24, pp. 851, 852 and 853)
Isobutane	Aluminum, 6 *M* × 3 mm I.D. 10% liquid G30 on nonacid washed S1C	Helium	33	TCD	None	NF (19, p. 2467)

(Continued)

Table 2 Compendial applications of GC for the assay of pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage form	Column	Carrier gas	Temp. (°C)	Detector	Internal standard	Reference
Isoamyl Methoxycinnamate	25 *M* × 0.32 mm I.D. coated G1 (0.1 μm)	Helium	60–240 8/min	FID	None	USP (24, p. 918)
Isoflurane	Nickel or Stainless Steel, 3.7 *M* × 2.4 mm I.D. 10% G31 + 15% G18 on S1C (60–80 mesh)	Heilium	65–110 4/min	FID	Butyl Acetate	USP (24, p. 920)
Isoflurophate Isoflurophate Ophthalmic solution	Glass, 1.8 *M* × 4 mm I.D. 5% G33/S1AB (80–100 mesh)	Helium	75–80	FID	Cyclohexanone	USP (24, pp. 921 and 922)
Isopropyl Alcohol	Stainless Steel, 1.8 *M* × 6.4 mm I.D. 10% liquid G20/S1A	Helium	55	TCD	None	USP (24, p. 927 and NF 19, p. 2468)
Isopropyl Myristate	1.8 *M* × 4 mm I.D. 10% liquid G8/S1 (100– 120 mesh)	Nitrogen	90–210 2/min	FID	None	NF (19, p. 2468)
Isopropyl Palmitate	1.8 *M* × 4 mm I.D. 10% liquid G8/S1 (100– 120 mesh)	Nitrogen	90–210 2/min	FID	None	NF (19, p. 2468)
Isosorbide	Glass, 0.6 *M* × 3 mm I.D. S9	Nitrogen	230	FID	Triethylene Glycol	USP (24, pp. 934 and 935)
Isosorbide oral solution						
Lindane cream	Glass, 1.8 *M* × 3 mm I.D. G3/S1A	Nitrogn	195	FID	n-Docosane	USP (24, pp. 976 and 977)
Lindane lotion						
Lindane shampoo						
Malathion lotion	Glass, 1.8 *M* × 2 mm I.D. 5% liquid G6/S1A (110–120 mesh)	Nitrogen	190	FID	Parathion	USP (24, p. 1012)
Menthol lozenges	30 *M* × 0.53 mm I.D. fused Silica coated with G16 (μm)	Helium	125	FID	Anethole in Hexanes	USP (24, p. 1038)
Menthyl Anthranilate	25 *M* × 0.32 mm I.D. Column coated with G1 (0.1 μm)	Helium	60–240 8/min	FID	None	USP (24, p. 1039)
Methadone Hydrochloride injection	Glass, 1.2 *M* × 4 mm I.D. 3% G2/S1A (10–20 mesh)	Helium	170	FID	Procaine	USP (24, p. 1057)
Methohexital Sodium for injection	1.2 *M* × 4 mm I.D. 3% G10/S1AB	Helium	230	FID	Aprobarbital	USP (24, p.1069)
Methoxyflurane	Stainless Steel, 3 *M* × 4 mm I.D. G11/S1A	Helium	100–110	TCD	None	USP (24, p. 1074)
Methyl Alcohol	Stainless Steel, 2 *M* × 3 mm O.D. S4 (50–80 mesh)	Nitrogen	140	FID	None	NF (19, p. 2479)
Methyl Benzylidene Camphor	30 *M* × 0.32 mm I.D. fused Silica capillary coated with G1 (0.25 μm)	Helium	100–230 10/min	FID	None	USP (24, p. 1077)

(Continued)

Table 2 Compendial applications of GC for the assay of pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage form	Column	Carrier gas	Temp. (°C)	Detector	Internal standard	Reference
Methylcellulose	1.8 *M* × 4 mm I.D. 10% liquid G1/S1A (100–120 mesh)	Helium	100	FID	Toluene	USP (24, p. 1079)
Methylene Chloride	1.8 *M* × 4 mm I.D. 15% liquid G18/Unsilanized S1C (30–60 mesh)	Helium	60	TCD	None	NF (19, p. 2480)
Methylparaben, Ethylparaben, Propylparaben, Butylparaben	Glass or Stainless Steel, 1.8 *M* × 2 mm I.D. 5% G2/S1A	Helium or Nitrogen	150	FID	Benzophenonle	USP (24, p. 1865)
Mibolerone oral solution	0.61 *M* × 3 mm I.D. 1% liquid G6/S1AB	Helium	175	FID	1,3,5-Triphenylbenzene	USP (24, p. 1112)
Miconazole Nitrate cream	1.2 *M* × 2 mm I.D. 3% G32/S1A	Helium	250	FID	Cholestane	USP (24, pp. 1114 and 1115)
Miconazole Nitrate topical powder Miconazole Nitrate vaginal suppositories						
Nitrogen Nitrogen 97 percent	3 *M* × 4 mm I.D. synthetic Alkali metal Aluminosilicate as a molecular sieve	Helium	Controlled	TCD	None	NF (19, p. 2485)
Octocrylene	60 *M* × 0.32 m I.D. column coated with G1 (0.25 μm)	Helium	80–280 4/min	FID	None	USP (24, p. 1213)
Octyldodecanol	2 *M* × 2 mm I.D. 3% G2/S1A	Nitrogen	80–300 6 min	FID	None	NF (19, p. 2286)
Octyl Methoxycinamate	25 *M* × 0.32 mm I.D. column with G1	Helium	None	FID	Benzyl Benzoate	USP (24, p. 1213)
Octyl Salicylate	25 *M* × 0.32 mm I.D. column coated with G1 (o.1 μm)	Helium	60–240 8/min	FID	None	USP (24, p. 1214)
Oxandrolone tablets	Glass, 2 *M* × 4 mm I.D. 3% Methyl Silicone oil on 80- to 10- mesh acid-, base- and water-washed, flux calcined, silanized sliceceous earth	Helium	250	FID	n-Octacosane	USP (24, p. 1225)
Penicillin G Procaine, Dihydrostrptomycin Sulfate, Chlorpheniramine Maleate, and Deaxmethasone injectable suspension (for Chlorpheniramine)	Glass, 1.8 *M* × 4 mm I.D. 1.2% G16 amd 0.5% KOH/S1A (10–120 mesh)	Nitrogen	180	FID	Brompheniramine Maleate	USP (24, p. 1281)
Pentobarbital elixir	Glass, 0.9 *M* × 4 mm I.D. 3 % liquid G10/S1A (80–10 mesh)	Nitrogen	190–210	FID	n-Tricosane	USP (24, p. 1293)
Pentobarbital Sodium capsules	Glass, 0.9 *M* × 4 mm I.D. 3 % liquid G10/S1A (80–10 mesh)	Nitrogen	190–210	FID	n-Tricosane	USP (24, p. 1295)
Perflubron	60 *M* × 0.25 mm I.D. G2 (1 μm)	Hydrogen	35–185 20/min	FID	None	USP (24, p. 1295)
Phendimetrazine Tartrate capsules	Glass, 1 *M* × 1 mm I.D. 3% G3/S1A	Helium	160	FID	Benzocaine	USP (p. 1055)

(Continued)

Table 2 Compendial applications of GC for the assay of pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage form	Column	Carrier gas	Temp. (°C)	Detector	Internal standard	Reference
Phendimetrazine Tartrate tablets						
Primidone oral suspension	Glass, 1.2 *M* × 4 mm I.D. 10% liquid G3/S1AB	Helium	260	FID	Androsterone	USP (24, pp. 1392 and 1393)
Primidone tablets						
Propane	Aluminum, 6 *M* × 3 mm I.D. 10% liquid G30 on non-acid washed S1C	Helium	33	TCD	None	NF (19, p. 2505)
Propoxyphene Hydrochloride, Aspirin and Caffeine capsules (for Propoxyphene and Caffeine	0.6 *M* × 3 mm I.D. 3% Methyl Phenyl Silicone liquid/80–10 mesh siliceous earth	Nitrogen	175	FID	n-Tricosane	USP (24, p. 1423)
Propoxyphene Napsylate oral suspension	Glass or Stainless Steel, 0.6 *M* × 3 mm I.D. 3% G2/S1AB	Helium	160	FID	n-Tricosane	USP (24, p. 1425)
Propoxyphene Napsylate tablets						
Propoxyphene Napsylate and Aspirin tablets (for Propoxyphene)	1.2 *M* × 3 mm I.D. 3% G3/ S1A	Nitrogen	175	FID	n-Tricosane	USP (24, p. 1427)
Propylene Glycol	Glass or Stainless Steel, 1 *M* × 4 mm I.D. 5% G16/S5	Helium	122–200 5/min	TCD	None	USP (24, p. 1434)
Scopolamine Hydrobromide injection	Glass, 1.8 *M* × 2 mm I.D. 3% liquid G3/S1AB	Nitrogen	225	FID	Homatropine Hydrobromide	USP (24, pp. 1507, 1508 and 1509)
Scopolamine Hydrobromide ophthalmic solution						
Scopolamine Hydrobromide ophthalmic ointment						
Scopolamine Hydrobomide tablets						
Secobarbital elixir	Glass, 0.9 *M* × 4 mm I.D. 3% G10/S1A (80–100 mesh)	Nitrogen	200	FID	Butabarbital	USP (24, pp. 1509 and 1510)
Secobarbital Sodium capsules						
Secobarbital Sodium and Amobarbital	Glass, 0.6 *M* × 3.5 mm I.D. 3% liquid G10/S1AB (100–120 mesh)	Helium	175	FID	Aprobarbital	USP 24, p. 1511)
Sodium capsules						
Spectinomycin Hydrochloride	Glass, 0.6 *M* × 3 mm I.D. 5% G27/S1AB (80–100 mesh)	Helium	190	FID	Tripheny-lanti-mony	USP (24, p. 1545)
Spectinomycin for injectable suspension	Glass, 0.6 *M* × 3 mm I.D. 5% G27/S1AB (80–100 mesh)	Helium	190	FID	Hexame-thyldi-silazane	USP (24, p. 1545)
Stearic Acid	Glass, 1.5 *M* × 3 mm I.D. 15% G4/S1A	Helium	165	FID	None	NF (19, p. 2525)

(Continued)

Table 2 Compendial applications of GC for the assay of pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage form	Column	Carrier gas	Temp. (°C)	Detector	Internal standard	Reference
Purified Stearic Acid Stearyl Alcohol	2 *M* × 3 mm I.D. 10% G2/S1A	Helium	205	FID	None	NF (19, p. 2526)
Terpin Hydrate	Glass, 1.2 *M* × 3.5 mm I.D. 6% G1/S1A	Nitrogen	120	FID	Biphenyl	USP (24, pp. 1607 and 1608)
Terpin Hydrate elixir Terpin Hydrate and Codeine elixir	Glass, 1.2 *M* × 3.5 mm I.D. 6% G1/S1A	Nitrogen	230	FID	Biphenyl and N-Phenylcarbazole	USP (24, p. 1608)
Testosterone Cypionate	Glass, 1.2 *M* × 3 mm I.D. 1% G6/S1AB	Helium	260	FID	Cholesteryl Caprylate	USP (24, pp.1610 and 1611)
Testosterone Cypionate injection Tetracaine and Menthol ointment	Glass, 1.8 *M* × 2 mm I.D. 10% G16/S1AB	Helium	170	FID	Decanol	USP (24, p. 1615)
Tiletamine and Zolazepam for injection	1.24 *M* × 4 mm I.D. 3% G2/S1AB (100–120 mesh)	Helium	150–230 10/min	FID	Tetraphenyle-thylene	USP (24, p. 1660)
Tocopherols excipient	Glass, 2 *M* × 4 mm I.D. 2–5% liquid G2/S1AB (80–1000 mesh)	Nitrogen	245–265	FID	Hexadecyl exa-decanoate	NF (19, p. 2531)
Tributyl Citrate	30 *M* × 0.32 mm I.D. G42 (0.5 μm)	Helium	80–225 20/min	FID	None	NF (19, p. 2532)
Trichloromono-fluormethane	Stainless Steel, 1.8 *M* × 2 mm I.D. 1% G25/S12	Helium	70–170 10/min	FID	None	NF (19, p. 2532)
Compound Undecylenic Acid ointment	Glass, 1.8 *M* × 2 mm I.D. 3% G1/S1A (100–20 mesh)	Helium	165	FID	Tridecanoic Acid	USP (24, p. 1729)
Valproic Acid	1.8 *M* × 2.0 mm I.D. 10% G34/S1A (80–100 mesh)	Helium	155	FID	Nonanoic Acid	USP (24, p. 1732)
Valproic Acid capsules	Glass, 1.8 *M* × 2 mm I.D. 10% G34/S1A (80–100 mesh)	Helium	150	FID	Biphenyl	USP (24, pp. 1733 and 1734)
Valproic Acid Syrup Vitamin E	Borosilicate glass, 2 *M* × 4 mm I.D. 2–5% liquid G2/S1AB 80–10 mesh)	Nitrogen	245–265	FID	Hexadecyl Hex-adecanoate	USP (24, pp. 1747 and 1749)
Vitamin E preparation Vitamin E capsules						
Vitamin E Polyethylene Glycol Succinate	5 *M* × 0.25 mm I.D. fused Silica capillary with G27 (0.25 μm)	Helium	260–340 20/min	FID	Ethyl Aracidate	NF (19, p. 2535)
Xylitol	30 *M* × 0.25 mm I.D. capillary with G46 (0.25 μm)	Helium	170°–215° 6/min 215–270 10/min	FID	Erythritol	NF (19, p. 2538)

Table 3 Compendial applications of GC for the chromatographic and radiochemical purity of pharmaceutical raw materials and dosage forms

Material/dosage form	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Alprazolam	Glass, 1.2 *M* × 3 mm I.D. 3% G6/S1AB	Helium	240	FID	None	USP (24, p. 64)
Amantadine Hydrochloride	Glass, 1.8 *M* × 2 mm I.D. G44/S1A (100–120 mesh)	None Specified	100–200 6/min	FID	None	USP (24, p. 103)
Avobenzene	Fused Silica 25 *M* × 0.32 mm Capillary Coated with G1	Helium	200–280 4/min	FID	None	USP (24, p. 181)
Chloroxylenol	Glass, 1.8 *M* × 4 mm I.D. 3% G16/S1A	Nitrogen	180	FID	None	USP (24, p. 391)
Clofibrate	15 *M* × 0.53 mm I.D. Capillary Coated with G1 (1.5 μm)	Helium	120–180 5/min	FID	None	USP (24, p. 442)
Dichlorodi-fluoromethane Dichlorotetrafluoroethane	Stainless Steel, 1.8 *M* × 2 mm I.D. 1% G25/S12	Helium	70–170 10/min	FID	None	NF (19, pp. 2445 and 2446)
Ethchlorvynol	Glass (pre-treated with 10% dimethyldichlorosilane in toluene),1.8 *M* × 4 mm I.D. 10% G16/S1AB (60–80 mesh)	Helium	160	TCD	None	USP (24, p. 691)
Ethyl Acetate	Glass, 1.8 *M* × 4 mm I.D. S11	Nitrogen	115–200 16/min	FID	None	NF (19, p. 2450)
Glycerin	30 *M* × 0.53 mm I.D. Fused Silica G43 (3 μm) with a 5 *M* × 0.53 mm I.D. Silica Guard Column (deactivated with phenylmethyl siloxane)	Helium	40–220 5/min	FID	None	USP (24, p. 780)
Halothane	Stainless Steel, 3 *M* × 2 mm I.D. 20% G24/S1AB	Nitrogen	60	FID	1,1,2-Trichloro-1,2,2-trifluoroethane	USP (24, p. 806)
Menthol	1.8 *M* × 2 mm I.D. 10% G16/S1AB	Helium	170	FID	Decanol	USP (24, p. 1038) and NF (19, p. 2477)

(Continued)

Table 3 Compendial applications of GC for the chromatographic and radiochemical purity of pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage form	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Meperidine Hydrochloride	Glass, 2 *M* × 2 mm I.D. 10% G3/S1A	Helium	190	FID	None	USP (24, p. 1039)
Mepivacaine Hydrochloride	Glass, 1.8 *M* × 4 mm I.D. 3% G19/S1A	Helium	230	FID	None	USP (24, p. 1041)
Nicotine	0.3 *M* × 0.53 mm I.D. fused Silica column bonded with G1(1.5 μm)	Helium	50–250 5/min	FID	None	USP (24, p. 1179)
Octyl Methoxycinamate	25 *M* × 0.32 m I.D. Column with G1	Helium	80–300 Linearly	FID	None	USP (24, p. 1213)
Water O 15 Injection (radiochemical purity)	Stainless Steel, 1.8 *M* × 3 mm I.D. S3 (80–100 mesh)	Helium	150	TC and Radioactivity	None	USP (24, p. 1240)
Padimate O	Stainless Steel, 1.8 *M* × 3 mm I.D. 10% liquid G9/S1A	Helium	150–250 10/min	FID	None	USP (24, p. 1252)
Perflubron	60 *M* × 0.25 mm I.D. G2 (1 μm)	Hydrogen	35–185 20/min	FID	None	USP (24, p. 1295)
Squalane	1.8 *M* × 3 mm I.D. 3% G1/S1A	Nitrogen	130–270 6/min	FID	None	NF (19, p. 2524)
Triazolam	Glass, 1.2 *M* × 3 mm I.D. 3% G6/S1AB	Helium	240	FID	None	USP (24, p. 1695)
Trichloromono-fluoromethane	Stainless Steel, 1.8 *M* × 2 mm I.D. 1% G25/S12	Helium	70–170 10 min	FID	None	NF (19, p. 2532)
Triclosan	15 *M* × 0.53 mm I.D. capillary with G3	Helium	34	FID	None	USP (24, p. 1700)
Valproic Acid	60 *M* × 0.32 mm I.D. coated with G25	Helium	145	FID	None	USP (24, p. 1732)

Table 4 Compendial applications of GC for the identification of pharmaceutical raw materials and dosage forms

Material/dosage form	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Acetyltributyl Citrate	30 *M* × 0.32 mm I.D. column bonded with G42 (0.5 μm)	Helium	80–220 20/min	FID	None	NF (19, p. 2409)
Acetyltriethyl Citrate						
Amitraz	1.5 *M* × 4 mm I.D. 3% G1/S1A	Nitrogen	250	FID	Squalane	USP (24, p. 121)
Amitraz Concentrate for dip						
Cetostearyl Alcohol	2 *M* × 3 mm I.D.10% liquid G2/S1	Helium	205	FID	None	NF (19, p. 2434)
Cetyl Alcohol	2 *M* × 3 mm I.D. 10% liquid G2/S1A	Helium	205	FID	None	NF (19, p. 2435)
Clioquinol	Glass, 1.83 *M* × 2 mm I.D. 3% G3/S1AB (80–100 mesh)	Helium	165	FID	Pyrene	USP (24, pp. 435, 436 and 437)
Cliquinol cream						
Clioquinol ointment						
Cliquinol and Hydrocortisone cream						
Cliquinol and Hydrocortisone ointment						
Colestipol Hydrochloride	Glass, 1.8 *M* × 3 mm I.D. 0.25% potassium hydroxide and 5%G16/S1A (80–100 mesh)	Helium	85	FID	None	USP (24, p. 465)
Dicyclomine Hydrochloride capsules	fused Silica 15 *M* × 0.5 mm coated with G3(1 μm)	Nitrogen	160–240 20/min	FID	Phenacetin	USP (24, pp. 549, 550 and 551)
Dicyclomine Hydrochloride injection						
Dicyclomine Hydrochloride syrup						
Dicyclomine Hydrochloride tablets						
Conjugated Estrogens	15 *M* × 0.25 mm I.D. fused Silica capillary bonded with G19 (0.25 μm)	Hydrogen	220	FID	3-O-Methyles-trone	USP (24, pp. 681, 582, 683 and 684)
Conjugated Estrogen tablets						
Esterified Estrogens						
Esterified Estrogen tablets						
Glyceryl Behenate	1.8 *M* × 4 mm I.D.10% liquid G27/S1A	Not specified	225	FID	None	NF (19, p. 2462)

(Continued)

Table 4 Compendial applications of GC for the identification of pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage form	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Guaifenesin and Codeine Phosphate syrup	0.6 *M* × 2 mm I.D.3% liquid G3/S1A (100–120 mesh) (For Codeine Phosphate)	Helium	210	FID	Hydrocodone Bitartrate	USP (24, p. 793)
Guaifenesin and Codeine Phosphate syrup	1.2 *M* × 4 mm I.D. 37% liquid G6/S1A (100–120 mesh) (For Guaifenesin)	Helium	170	FID	Dipropyl Phthalate	USP (24, p. 793)
Hydrocortisone and Acetic Acid Otic solution	Glass, 1.8 *M* × 2 mm I.D. 20% liquid G35/S1A	Nitrogen	115–190 35/min	FID	Anisole	USP (24, p. 827)
Isosorbide oral solution	Glass, 0.6 *M* × 3 mm I.D. S9	Nitrogen	230	FID	Triethylene Glycol	USP (24, p. 935)
Perflubron	60 *M* × 0.25 mm I.D. G2 (1μm)	Hydrogen	35–185 20/min	FID	None	USP (24, p. 1295)
Triclosan	15 *M* × 0.53 mm I.D. capillary with G3	Helium	34	FID	None	USP (24, p. 1700)
Valproic Acid	1.8 *M* × 2.0 mm I.D. 10% G34/S1A (80–100 mesh)	Helium	155	FID	Nonanoic Acid	USP (24, p. 1732)
Valproic Acid capsules Valproic Acid syrup	Glass, 1.8 *M* 7 × 2 mm I.D. 10% G34/S1A (80–100 mesh)	Helium	150	FID	Biphenyl	USP (24,pp. 1733 and 1734)
Vitamin E Vitamin E Preparation Vitamin E capsules	Glass, 2 *M* × 4 mm I.D. 2–5% liquid G2/S1AB (80–10 mesh)	Nitrogen	245 –265	FID	Hexadecyl Hexadecanoate	USP (24,pp. 1747 and 1749)
Vitamin E Vitamin E preparation Vitamin E capsules	Glass, 2 *M* × 4 mm I.D. 2–5% liquid G2/S1AB (80–10 mesh)	Nitrogen	245 –265	FID	Hexadecyl Hexadecanoate	USP (24,pp. 1747 and 1749)
Vitamin E Polyethylene Glycol Succinate	15 *M* × 0.25 mm I.D. fused Silica capillary with G27 (0.25 μm)	Helium	260–340 20/min	FID	Ethyl Aracidate	NF (19, p. 25s35)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Amoxicillin	Dimethylaniline	2 *M* X 2 mm I.D. 3% G3/silanized S1A	Nitrogen	120	FID	Napthalene	USP (24, p. 129)
Ampicillin	Dimethylaniline	2 *M* X 2 mm I.D. 3% G3/silanized S1A	Nitrogen	120	FID	Napthalene	USP 24, p. 136)
Ampicillin Sodium	Dimethylaniline	2 *M* × 2 mm I.D. 3% G3/silanized S1A	Nitrogen	120	FIDN	N-Diethylaniline	USP (24, p. 140)
Ampicillin Sodium	Methylene Chloride	glass, 1.8 *M* × 4 mm I.D. 10% 39/S1A	Nitrogen	65	FID	Dioxane	USP (24, p. 140)
Amyl Nitrite	Total Nitrites	2 *M* × 3 mm I.D. 25% methyl polysiloxane on suitable calcined diatomate	Helium	80	TCD	None	USP (24, pp. 144 and 145)
Amyl Nitrite inhalant							
Bacampicillin Hydrochloride	Dimethylaniline	2 *M* × 2 mm I.D. 3% G3/silanized S1A	Nitrogen	120	FID	Napthalene	USP (24, p. 189)
Benzethonium Chloride Tincture	Acetone and Alcohol	1.2 *M* × 4 mm S3 (80–100 mesh)	Helium	120	FID	Methanol	USP (24, p. 204)
Brompheniramine Maleate	Related substances	Glass, 1.2 *M* × 4 mm I.D. 3% G3/S1AB	Helium	190	FID	None	USP (24, p. 251)
Bupivacaine Hydrochloride	Residual solvents	2 *M* × 6 mm I.D. S3	Nitrogen	175	FID	None	USP (24, p. 256)
Butyl Alchohol	Butyl Ether	Stainless steel, 2 *M* × 6 mm l.D.25% liquid G29 3,3' thiodipropionitrile/ S1C (30–40 mesh)	Helium	85	TCD	None	NF (19, p. 2422)
Carbomer 910	Benzene	30 *M* × 0.53 mm I.D. fused Silica analytical column with G34 (3.0 μm)and a 5 *M* × 0.53 mm l.d. guard column deactivated with Phenylmethyl Siloxane	Helium	40 – 260 50/min	FID	None	NF (19, pp. 2426, 2427 and 2428)

(Continued)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms (*Continued*)

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Carbomer 934 Carbomer 934P Carbomer 940 Carbomer 941 Carbomer 1342							
Cefadroxil	Dimethylaniline	2 *M* × 2 mm I.D. 3% G3/silanized S1A	Nitrogen	120	FID	Napthalene	USP (24, p. 326)
Cefoxitin Sodium	Acetone and Methanol	Glass, 1.8 *M* × 6.3 mm I.D. S2, silane treated 60–80 mesh glass beads precolumn	Nitrogen	110	FID	None	USP (24, p. 345)
Cephalexin	Dimethylaniline	2 *M* × 2 mm I.D. 3% G3/silanized S1A	Nitrogen	120	FID	Napthalene	USP (24, p. 361)
Cephalexin Hydrochloride Maleate	Related substances	Glass, 1.2 *M* × 4 mm I.D. 3% G3/S1AB	Helium	190	FID	None	USP (24, p. 392)
Maleate Ciclopirox Olamine Cream Ciclpirox Olamine Topical suspension	Benzyl Alcohol	Glass, 2 *M* × 4 mm I.D. 3% G3/S1AB(100–120 mesh)	Nitrogen	100	FID	1-Nonyl Alcohol	USP (24, pp. 410 and 411)
Cilastin Sodium	Acetone, Methanol and Mesityl Oxide	30 *M* × 0.53 mm capillary, Gl6 1μ film	Helium	50–70 8/min	FID	n-Propyl Alcohol	USP (24, p. 411)
Clavulanate Potassium	Methanol and tert-butylamine	30 *M* × 0.32 mm capillary, G1	Nitrogen	40 – 200 55/min	FID	None	USP (24, p. 426)
Clofibrate	p-chlorophenol	15 M × 0.53 mm I.D. capillary coated with Gl (l.5 m)	Helium	120 –180 5/min	FID	None	USP (24, p. 442)
Cloxacillin Sodium	Dimethylaniline	2 *M* × 2 mm I.D. 3% G3/silanized S1A	Nitrogen	120	FID	Napthalene	USP (24, p. 456)
Colchicine	Residual Chloroform and Ethyl Acetate	Glass or Stainless Steel, 1.5 *M* × 4 mm l.D.20% G14/S1	Nitrogen	75	FID	n-Propanol	USP (24, p. 464)

(Continued)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms (*Continued*)

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Collodion	Alcohol	Glass,1.8 *M* × 3.5mm I.D. S3	Helium	150	TCD	1,2-Dichloroethane	USP (24,P. 469)
Flexible collodion							
Cyclosporine injection	Alcohol	Glass, 2 *M* × 2 mm I.D. S3	Nitrogen	145–270 32/min	FID	n-Propyl Alcohol	USP (24, pp. 488 and 489)
Cyclosporine oral solution							
Cyclosporine injection Cyclosporine oral solution	Alcohol	Glass, 2 *M* × 2 mm I.D. S3	Nitrogen	145–270 32/min	FID	n-Propyl Alcohol	USP (24, pp. 488 and 489)
Desflurane	Related compounds and Trichlorofluoromethane, Dichlorofluoromethane, Methylene Chloride, Chloroform, Trichlorotrifluoroethane and Isoflurane	Stainless Steel, 6.1 *M* × 2.4 mm I.D. 25% G16/S1A (80–100 mesh)	Helium	75	FID	None	USP (24, p. 504)
Dexbrom-pheniramine Maleate	Related substances	Glass, 1.2 *M* × 4 mm I.D. 3% G3/S1AB	Helium	190	FID	None	USP (24, p. 520)
Maleate	Related substances	Glass, 1.2 *M* × 4 mm I.D. 3% G3/S1AB	Helium	190	FID	None	USP (24, p. 520)
Maleate							
Dexpanthenol	Pantolactone	1.8 *M* × 2 mm I.D. 5% G2/S1A	Helium or Nitrogen	170	FID	2,6-Dimethylphenol	USP (24, p. 523)
Preparation							
Dextran 40 Dextran 70	Alcohol and related impurities	1.8 *M* × 2 mm I.D. S3	Nitrogen	160	FID	None	USP (24, pp. 523 and 526)
Dextran 70							
Dicloxacillin Sodium	Dimethylaniline	2 *M* × 2 mm I.D. 3% G3/silanized S1A	Nitrogen	120	FID	Napthalene	USP (24, p. 548)
Diethylene Glycol Monoethyl Ether	Ethylene Oxide	Glass or Quartz, 30 *M* × 0.32 mm I.D. capillary with G1 (1.0 μm)	Helium	50 – 180 5/min 180–230 30/min	FID	None	NF (19, p. 2447)

(Continued)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms (*Continued*)

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Diethylene Glycol Monoethyl Ether	Ethylene Oxide	Glass or Quartz, 30 *M* × 0.32 mm I.D. capillary with G1 (1.0 μm)	Helium	50 – 180 5/min 180–230 30/min	FID	None	NF (19, p. 2447)
Dihydroxyaluminum Sodium Carbonate	Isopropyl Alcohol	0.9 *M* × 3 mm I.D. S3		180	FID	None	USP (24, p. 572)
Dimethyl Sulfoxide	Dimethyl Sulfone	1.5 *M* × 3 mm I.D. 10% liquid phase G25/ S1A	Helium	100–170 10/min	FID	Dibenzyl	USP (24, p. 579 and USP 24-NF 19 First Suppt, p. 2608
Doxylamine Succinate	Secondary peaks	2 *M* × 4 mm I.D. 5%G16, 5% G12/S1A (60–80 mesh)	Helium	212	FID	None	USP (24, p. 612)
Dyphylline elixir Dyphylline and Guaifenesin elixir	Alcohol	Glass, 0.75 *M* × 4 mm I.D. 20% G20/S1AB	Nitrogen	85	FID	None	USP (24, pp. 618 and 619)
Conjugated Estrogens Esterified Estrogens	Estrone, Equilin and 17α-dihyroeuilin (free steroids)	15 *M* × 0.25 mm I.D. fused Silica capillary bonded with G19(0.25 μm)	Hydrogen	220	FID	3-O-Methylestrone	USP (24, pp. 681 and 683)
Ether	Low-boiling hydrocarbons	Stainless Steel, 3.7 *M* × 2 mm I.D 30%G22/S1C (30–60 mesh)	Nirtrogen	80	FID	None	USP (24, p. 692)
Ethosuximide	2-Ethyl-2-methylsuccinic Anhydride and other impurities	1.8 *M* × 6.4 mm I.D. 5% G5/ S1A (60–80 mesh)	Helium	140	HFD	None	USP (24, p. 695)
Etodolac	Alcohol and Methanol	25 *M* × 0.32 mm I.D. fused Silica capillary G36 (5 μm)	Helium	45–280 30/min	FID	Isopropyl Alcohol	USP 244, p. 701)

(Continued)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms (*Continued*)

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Fluocinonide topical solution	Alcohol content	Glass, 1.8 *M* × 2 mm I.D. S3 (80–120 mesh)	Nitrogen or Helium	130	FID	Isopropyl Alcohol	USP (24, p. 729)
Gadodiamde	Acetone, Ethyl Alcohol, Isopropyl Alcohol	30 *M* × 0.32 mm I.D. capillary with G43 (1.8 μm)	Helium	40	FID	Methyle Ethyl Ketone	USP (24 - NF 19 First Suppl,P. 2618
Gentamicin Sulfate	Methanol	1.5 *M* × 4 mm I.D. S3	Nitrogen	120 – 140	FID	n-Propyl Alcohol	USP (24, p. 765)
Glycerin	Methylene Chloride, Benzene, Trichloroethylene, 1,4-Dioxane, Chloroform, Heuylene Glycol	30 *M* × 0.53 mm I.D. fused Sillica G43 (3 μm) with a 5 *M* × 0.53 mm l.D. Sillica guard column (deactivated with phenylmethyl siloxane)	Helium	40–220 5/mm	FID	None	USP (24, p. 780 and NF 19, p. 2461)
Glyceryl	Free Glycern	Glass, 2.4 *M* × 4 mm I.D. 2% liquid G16/S1A (80–100 mesh)	Helium	190 – 200	FID	Tributyrin	NF (19, p. 2463)
Monostearate Glyceryl	Monoglycerides	Glass, 2.4 *M* × 4 mm I.D. 2% liquid G27/S1A (80–100 mesh)	Helium	270 – 280	FID	Hexadecyl Hexadecanoate	NF (19, p. 2463)
Monostearate Guaifenesin and Codeine Phosphate syrup	Alcohol content	1.8 *M* × 2 mm I.D. 5% liquid G16/S1A (100–120 mesh)	Helium	50–100 20/min	FID	Acetone	USP (24, p. 793)
Guanabenz Acetate	2,6-dichlorobenzaldehyde	Glass, 1.8 *M* × 3 mm I.D. 20% G1/SlA (80–100 mesh)	Nitrogen	190	FID	p-Chlorobenzaldehyde	USP (24, p. 796)
Hexachlorophene	2,3,7,8-tetrachlorodibenzo-p-dioxin	Glass, 1 *M* × 2 mm I.D. Gl/Sl	Helium	250	Mass Spectrograph	None	USP (24, p. 810)
Hydrocortisone and Acetic Acid otic solution	Acetic Acid	Glass, 1.8 *M* × 2 mm I.D. 20% liquid G35/SlA	Nitrogen	115–190 35/min	FID	Anisole	USP (24, p. 827)

(Continued)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms (*Continued*)

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Ifosfamide	2-chloroethylamine hydrochloride	1.8 *M* × 2 mm I.D. 10% liquid G16,2%KOH/SlA (80–100 mesh)	Nitrogen	140°	FID	None	USP (24, p. 861)
Imipenem	Acetone, Isopropyl Alcohol	1.8 *M* × 3 mm I.D. 10% G16/S5	Helium	70–170 32/min	FID	n-Propyl Alcohol	USP (24, p. 863)
Indomethacin Sodium	Acetone	Glass, 1.8 *M* × 3 mm I.D. S3	Nitrogen	165	FID	None	USP (24, p. 878)
Iohexol	Methanol, Isopropyl Alcohol, Methoxyethanol	Glass, 2 *M* × 2 mm I.D. S6	Nitrogen	125 – 225 Maximum Rate	FID	None	USP (24, p. 900)
Iopromide	Alcohol (limit)	30 *M* × 0.25 mm I.D. capillary coated liquid G43 (1.4 μm)	Helium	40–70 5/min 70–220 30/min	FID	None	USP (24, p. 904)
Ioxilan	Residual Methanol	10 *M* × 0.53 mm I.D. fused Silica capillary/S2	Helium	45–80 5/min	FID	Dehydrated Alcohol	USP (24, p. 911 and 912)
Ioxilan injection							
Iron dextran injection	Phenol (limit)	1.2 *M* × 3 mm I.D. 5% G16/S1A	Helium or Nitrogen	145	FID	Benzyl Alcohol	USP (24, p. 916)
Isoflurane	Acetone, 1-chloro-2,2,2-trifluoroethyl-chlorodi-fluoro- methy ether 2,2,2-trifluorethyl-difluor-methyl ether	Nickel or Stainless Steel, 3.7 *M* × 2.4 mm l.D.10%G31+ 15%G18 on S1C (60–80–nesh)	Helium	65–110 4/min	FID	Butyl Acetate	USP 24, p. 920
Azeotropic Isopropyl Alcohol	Air, Diethyl Ether, Diisopropyl Ether, Acetone, Isopropyl Alcohol, 2-Butanol, n-Propyl Alcohol, Water	Stainless Steel, 1.8 M × 6.4 mm l.D. 10% liquid G20/S1A	Helium	55	FID	None	USP 24, p. 927
Isosorbide	Methyl-ethyl Ketone	Glass or Stainless Steel, 0.6 M × 2 mm l.D. 25% G16 On Unsilanized S1A	Nitrogen	70	FID	Methyl-isobutyl Ketone	USP 24, p. 934
Isoxsuprine	Related compounds	Glass, 2 M × 3 mm I.D. 3% liquid G3/S1A	Nitrogen	215	FID	None	USP 24, p. 940

(Continued)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms (*Continued*)

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Hydrochloride							
Lanolin	Diazinon, Diclofenthion, Bromophos ethyl, lindane, Dieldrin	System I: 30M × 053 mm I.D. fused Sillica bonded with G1 (1.5 μ m) and a 6 M × 0.53 mm I.D. uncoated guard column System II: 30 M × 0.53 mm I.D. Fused Silica Capillary Bonded with G3 (1 μm) and a 6 M × 0.53 mm I.D. uncoated guard column	Helium	200°	ECD Flameiphotometroc Detector	Chlorpyrifos	USP 24, p. 953
Modified Lanolin	Free Lanolin Alcohols	50 M × 0.33 mm I.D. fused Silica capillary bonded with G2 (0.5 μ m) with a 0.5 M × 0.32 mm I.D. uncoated guard column	Nitrogen	210 – 280 3/min	FID	None	USP 24, p. 955and NF 19,P. 2471
Levopropoxyphene Napsylate	Acetoxy Analog Napsylate	Glass, 0.6 M × 3 mm I.D. 3% G2/SlAB	Helium	160	FID	n-Tricosane	USP, p. 706
Magnesium Stearate	Stearic Acid, Palmitic Acid	30 M × 0.32 mm I.D. fused Silica with G16 (0.5 μm)	Helium	70 – 240 5/min	FID	None	NF 19, p. 2474
Malathion lotion	Isopropyl Alcohol	Glass, 1.8 M × 2 mm I.D. S2(110–120 mesh)	Nitrogen	130	FID	Ethylacetate	USP 24, p. 1012
Mesalamine	Aniline, 4-Aminophenol, 2-Aminophenol	10 M × 0.53 mm I.D. fused Sillica capillary coated with G27 (2.65 μm)	Helium	70 –150 30/min	FID	None	USP 24, p. 1045 and USP 24-NF 19 first Suppt, p. 2640
Metaproterenol Sulfate	Isopropyl Alcohol, Methanol	2 M × 2 mm I.D. 0.1% liquid G25/S7 (80–10 mesh)	Helium	40–200 15/min	FID	None	USP 24, p. 1051
Mitoxantrone	Alcohol	Glass, 3 M × 2 mm I.D. 20% G1 and 0.1%	Helium	50–140 30/min	FID	n-Propyl Alcohol	USP 24, p. 1121

(Continued)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms (*Continued*)

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Hydrochloride							
		G39/Silanized SlA					
Mono- and Diglycerides	Free Glycerin	Glass, 2.4 M × 4 mm I.D. 2% liquid G16/SlA (80–100 mesh)	Helium	190 –200	FID	Tributyrin	NF 19, p. 2483
Mono- and Diglycerides	Monoglycerides	Glass, 2.4 M × 4 mm I.D. 2% liquid G27/ SlA (80–100 mesh)	Helium	270 – 280	FID	Hexadecyl Hexadecanoate	NF 19, p. 2483
Moricizine Hydrochloride	Alcohol	Glass, 1.8 M × 4 mm I.D. S2	Helium	150	FID	None	USP 24, p. 1129
Myristyl Alcohol	Hydroxyl value	Glass, 2 M × 3 mm I.D. 10% G2/SlA	Helium	205	FID	None	NF, p. 1952
Naftifine Hydrochloride Gel	Alcohol	1.5 M × 3.2 mm I.D. S3 (80–100 mesh)	Nitrogen	170	FID	n-Propyl Alcohol	USP 24, p. 1139
Naltrexone Hydrochloride	Total Solvents (Alcohol and Methanol)	Glass, 1.8 M × 4 mm I.D. S3 (80–100 mesh)		150	FID	Isopropyl Alcohol	USP 24, p. 1143
Nonoxynol 9	Free ethylene oxide	Nickel, 6.4 M × 2.1 mm I.D. S9 (60–80 mesh)	Helium	100	FID	None	USP 24, p. 1194 and NF 19,P 2486
Nonoxynol 9	Dioxane	Glass, 1.8 M × 2 mm I.D. S10	Nitrogen or Helium	140	FID	None	USP 24, p. 1194, NF 19,P 2486 and USP 24-NF 19 First Suppt,P 2725
Octoxynol	Free ethylene oxide	Nickel, 6.4 M × 2.1 mm I.D. S9 (60–80 mesh)	Helium	100	FID	None	NF 19, p. 2486
Octoxynol 9	Dioxane	Glass, 1.8 M × 2 mm I.D. S10	Nitrogen or Helium	140	FID	None	NF 19, p. 2486 and USP 24-NF 19 First Suppt, P. 2725
Ofloxacin	Methanol, Ethanol	30 M × 0.53 mm I.D. fused Silica column coated with G43 (3 μm)	Helium	35 – 90 20/min 90–200 40/min	FID	n-Propyl Alchohol	USP 24, p. 1215
Oxycodone Hydrochloride	Alcohol	Glass, 1.8 M × 4 mm I.D. S3 (10–120 mesh)	Helium	150	FID	Isopropyl Alcohol	USP 24, p. 1233
Phenytoin Sodium injection	Propylene Glycol and Alcohol	Glass, 1.8 M × 2.0 mm I.D. silanised S3 (50–80 mesh)	Helium	140–190 6/min	FID	Ethylene Glycol and Methanol	USP 24, p. 1326

(Continued)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms (*Continued*)

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Polycarbophil	Ethyl Acetate	10 ft × 2 mm I.D. 1% G25/S12	Helium	160	FID	Methyl Ethyl Ketone	USP 24, p. 1348
Poloxamer	Limit of Free Ethylene Oxide Propylene Ooxide, 1,4 dioxane	50 *M* × 0.32 mm I.D. fused Silica with G27 (5 μm)	Helium	70–240 10/min	FID	None	NF 19, p. 2492 and USP 24-NF 19 First Suppt,P. 2725
Polyethylene Glycol	Limit of Free Ethylene Oxide and 1,4 dioxane	50 M × 0.32 mm I.D. fused Silica with G27 (5 μm)	Helium	70–250 10/min	FID	None	NF 19, p. 2493 and USP 24-NF 19 First Suppt,P. 2726
Polyethylene Glycol	Ethylene Glycol and Diethylene Glycol	Stainless Steel, 1.5 M × 3 mm l.D.12% G13/S1NS	Nitrogen	165	FID	None	NF 19, p. 2493
Polyethylene Glycol Monomethyl Ether	Ethylene Oxide and 1,4 dioxane	50 M × 0.32 mm I.D. fused Silica with G27 (5 xμm)	Helium	70 – 250 10/min	FID	None	NF 19, p. 2495
Polyethylene Glycol Monomethyl Ether	Ethylene Glycol and Diethylene Glycol	1M × 3mm I.D. S2 (60–80 mesh)	Nitrogen	200	FID	None	NF 19, p. 2495
Polyethylene Glycol Monomethyl Ether	2-methoxyethanol	15 M × 0.53 mm I.D. fused Silica capillary column with G16 (1 μm)	Helium	70–250 10/min	FID	None	NF 19, p.2495
Polyethylene Oxide	Free Ethylene Oxide	10 M × 0.53 mm I.D. Capillary Column with G45 (20 μm)	Helium	70–200 10/min	FID	None	NF 19, p. 2497
Polyoxyl 10 Oleyl Ether	Free Ethylene Oxide	Stainless Steel, 1.8 M × 3 mm I.D. (OD) S3	Helium	160	FID	n-Butyl Chloride	NF 19, p. 2498
Polyoxyl 20 Cetostearyl Ether	Free Ethylene Oxide	Stainless Steel, 1.8 M × 3 mm I.D. (OD) S3	Helium	160	FID	n-Butyl Chloride	NF 19, p. 2499
Procyclidine Hydrochloride	Related compounds	Glass 1 M × 2 mm I.D. 10% PEG 20,000 and 2% KOH/S1A	Helium	180	FID	None	USP 24, p. 1406
Propafenone Hydrochloride	Methanol, Acetone	30 *M* × 0.53 mm I.D. fused Silica column with G43 (3 μm) and a 5 M × 0.53 mm I.D. Silica guard column deactivated with Phenylmethyl Siloxane	Helium	40–240 Rapidly	FID	None	USP 24, p. 1414

(Continued)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms (*Continued*)

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Propoxyphene Hydrochloride	α-d-2-Acetoxy-4-dimethylamino-1,2-diphenyl-3-methylbutane, Carbinol hydrochloride, α-d-4-Dimethylamino-1,2-diphenyl-3-methyl-2-butanol hydrochloride	Glass or Stainless Steel, 0.6 M × 3 mm I.D. 3% G2/ S1 AB	Helium	160	FID	n-Tricosane	USP 24, p. 1420
Propoxyphene Napsylate	α-d-2-Acetoxy-4-dimethylamino-1,2-diphenyl-3-methylbutane, Carbinol hydrochloride, α-d-4-Dimethylamino-1,2-diphenyl-3-methyl-2-butanol hydrochloride	Glass or Stainless Steel, 0.6 M × 3 mm. I.D. 3% G2/S1 AB	Helium	160	FID	n-Tricosane	USP 24, p. 1424
Saccharin	Toluenesul-fonamides	Glass, 1.8 M × 3.2 mm I.D. 10% liquid G3/S1AB (100–120 mesh)	Helium	210	FID	n-Tricosane	NF 19, p. 2509
Saccharin Calcium	Toluenesul-fonamides	Glass, 1.8 M × 3.2 mm I.D. 10% liquid G3/S1AB (100–120 mesh)	Helium	210	FID	n-Tricosane	USP 24, p. 1497
Saccharin Sodium	Toluenesul-fonamides	Glass, 1.8 M × 3.2 mm I.D. 10% liquid G3/S1AB (100–120 mesh)	Helium	210	FID	n-Tricoasane	USP 24, p. 1498 and NF19, p. 2509
Salsalate	Dimethylaniline	30 M × 0.53 mm I.D. capillary coated with G42 (1 μm)	Helium	105	FID	Indene	USP 24, p. 1502
Salsalate	Isopropyl, ethyl and methyl salicylates	30 M × 0.53mm I.D. capillary coated with G42 (1 μm)	Helium	120	FID	None	USP 24, p. 1502
Sucralfate	Pyridine, 2-methylpyridine	10 M × 0.53 mm I.D. capillary coated with G27 (2.65 μm)	Helium	50	FID	3-Methylpyridine	USP 24, p. 1555
Sucralose	Methanol	Glass, 2 M × 4 mm I.D. silanized S6 (80–100 mesh)	Helium	150	FID	n-Propyl Alchohol	NF 19, p. 2527

(Continued)

Table 5 Compendial applications of GC for the presence of volatile matter, intermediates, and related substances in raw materials and dosage forms (*Continued*)

Material/dosage forms	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Sufentanil Citrate	Acetone	Glass, 1.83 M × 4 mm I.D. S2	Nitrogen	175	FID	None	USP 24 - NF 19 First Suppl, p. 2658
Tamoxifen Citrate	Related impurities	Glass, 1 M × 4 mm I.D. 5% liquid G17/S1AB (100– 120 meash)	Helium	260	FID	None	USP 24, p. 1586
Ticarcillin Disodium Ticarcillin Monosodium	Dimethylaniline	2 M × 2 mm I.D. 3% G3/silanized S1A	Nitrogen	120	FID	Napthalene	USP 24, p. 1657 and 1659
Tilmcosin injection	Propylene Glycol	15 M × 0.53 mm I.D. fused Silica with liquid G16 (1 μm)	Helium	100	FID	Pentadecane	USP 24, p. 1662
Triclosan	Related compounds	15 M × 0.53 mm I.D. capillary with G3	Helium	34	FID	None	USP 24, p. 1700
Triclosan	2,3,7,8-tetrachlorodibenzo-p-dioxin, 2,3,7,8-tetrachlorodibenofuran	30 M × 0.53 mm I.D. capillary with G3	Helium	80 –180 20/min 180–270 4/min	Mass Spec with electron impact ionization	C Tetrachloro-dibenzo-p-13 labelled 2,3,7,8-dioxin, C13 Labelled 2,3,7,8-Tetrachloro-dibenofuran	USP 24, p.1700
Warfarin Sodium	Isopropyl Alcohol	Glass, 1.8 M × 4 mm I.D. S2 (80–100 mesh)	Nitrogen	140	FID	n-Propyl Alcohol	USP 24, p. 1750
Xanthan gum	Isopropyl Alcohol	Stainless Steel, 1.8 M × 3.2 mm I.D. silanized S3 (80– 100 mesh)	Helium	165	FID	Tertiary Butyl Alcohol	NF 19, p. 2537
Xylazine	Acetone, Isopropyl Alcohol	1.8 M × 2mm I.D. 0.1% G25/ S7 (80– 10 mesh)	Helium	30–100 10/min 100–220 15/min	FID	None	USP 24, p. 1756
Xylitol	Other Polyols	30 M × 0.25 mm I.D. capillary with G 46 (0.25 μm)	Helium	170–215 6/min 215–270 10/min	FID	Erythritol	NF 19, p.2538

Table 6 Compendial applications of GC for the determination of water in pharmaceutical raw materials and dosage forms

Material/dosage form	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Acetone	Stainless Steel, 1.5 *M* × 6 mm I.D. S4	Helium	180	TCD	None	NF (19, p. 2409)
Echothiophate Iodide for Ophthalmic Solution	Glass, 1.8 *M* × 2 mm I.D. silanised S3 (80–100 mesh)	Helium	115	TCD	Anhydrous Methanol	USP (24, p. 621)
Gonadorelin Hydrochloride	Glass, 1.8 *M* × 2 mm I.D. S3 (80–100 mesh)	Helium	100	TCD	Anhydrous Methanol	USP (24, p. 784)

Table 7 Compendial applications of GC for the presence of isomers, isomeric purity, and racemate ratios in pharmaceutical raw materials

Material	Analyte	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Butorphanol Tartrate	Purity and presence of α-isomer	Glass, 1.8 *M* × 4 mm I.D. 3% G3/S1	Nitrogen	250	FID	None	USP (24,p. 271)
Ethchlorvynol	E-Ethchlorvynol	Glass (pretreated with 10% dimethyldichlorosilane in toluene), 1.8 *M* × 4 mm I.D. 10% G16/S1AB (60–80 mesh)	Helium	160	TCD	None	USP (24, p. 691)
Fludeoxyglucose F 18 injection	Isomeric purity	1.8 *M* × 3 mm I.D. 4% G2 (SF-30),6% G6 (OV 210)/S1A (80–100 mesh) (Chromosorb W-HP)	Helium	150	FID	None	USP (24, p. 733)
Labetalol Hydrochloride	Racemate ratio	Glass, 1.8 *M* times; 2 mm I.D. 10% G3/S1AB (10–120 mesh)	Nitrogen	320	FID	None	USP (24, p. 949)
Anhydrous Lactose	Content of alpha and beta anomers	Glass, 0.9 *M* × 4 mm I.D. 3% liquid G19/S1A	Helium	215	FID	None	NF (19, p. 2470)
Phendimetrazine Tartrate	L-erythro isomer	25 *M* × 0.25 mm I.D. capillary column G1 (0.4 μm)	Helium	140	FID	None	USP (24, p. 1301)

Table 8 Compendial applications of GC for the determination of alcohol content in raw materials and dosage forms[a]

Dosage form	Reference
Acetaminophen oral solution	USP (24, p. 18)
Oral solution containing at least three of the following—Acetaminophen and salts of Chlorpheniramine, Dextromethorphan, and Phenylpropanolamine	USP (24, p. 24)
Oral solution containing at least three of the following—Acetaminophen and salts of Chlorpheniramine, Dextromethorphan, and Pseudoephedrine	USP (24, p. 31)
Acetaminophen and Codeine Phosphate oral solution	USP (24, p. 35)
Acetaminophen, Dextromethorphan, Hydrobromide, Doxylamine Succinate, and Pseudoephedrine Hydrochloride oral solution	USP (24, p. 37)
Aminobenzoic Acid gel and topical solution	USP (24, p. 110 and, p. 111)
Aromatic elixir	NF (p. 1901)
Belladonna tincture	USP (24, p. 201)[b]
Compound Benzoin tincture	USP (24, p. 211)
Butabarbital Sodium elixir	USP (24, p. 262)
Camphor spirit	USP (24, p. 293)
Aromatic Cascara fluid extract	USP (24, p. 322)
Aromatic elixir	NF (19, p. 2415)
Cinoxate Lotion	USP (24, p. 416)
Desoximetasone gel	USP (24, p. 508)[c]
Dexamethasone elixir	USP (24, p. 512)
Dexamethasone Sodium Phosphate	USP (24, p. 516)[d]
Dexamethasone Sodium Phosphate inhalation aerosol	USP (24, p. 517)
Ergoloid Mesylates oral solution	USP (24, p. 656)
Erythromycin topical solution	USP (24, p. 667)
Etoposide injection	USP (24, p. 704)
Green Soap tincture	USP (24, p. 788)
Isoetharine Mesylate inhalation aerosol	USP (24, p. 919)
Isoproterenol Hydrochloride inhalation	USP (24, p. 928)[d]
Methdilazine Hydrochloride syrup	USP (24, p. 1061)
Methylcellulose oral solution	USP (24, p. 1080)
Nitroglycerin injection	USP (24, p. 1190)
Nortriptyline Hydrochloride oral solution	USP (24, p. 1206)
Opium tincture	USP (24, p. 1221)
Oxycodone Hydrochloride oral solution	USP (24, p. 1234)[b]
Paregoric	USP (24, p. 1263)
Peppermint spirit	USP (24, p. 1295)
Phenobarbital elixir	USP (24, p. 1306)
Potassium Chloride oral solution	USP (24, p. 1358)[b]
Potassium Gluconate elixir	USP (24, p. 1365)
Prednisilone syrup	USP (24, p. 1381)
Prednisone oral solution	USP (24, p. 1388)
Prednisone syrup	USP (24, p. 1389)
Propoxyphene Napsylate oral suspension	USP (24, p. 1425)
Pseudoephedrine Hydrochloride, Carbinoxamine Maleate, and Dextromethorphan Hydrobromide oral solution	USP (24) NF 19 First Suppl, p. 2654)
Resorcinol and Sulfur lotion	USP (24, p. 1478)
Sulfamethoxazole and Trimethoprim oral suspension	USP (24, p. 1573)
Terpin Hydrate elixir Terpin Hydrate and Codeine elixir	USP (24, pp. 1607 and 1608)
Theophylline and Guaifenesin oral solution	USP (24, p. 1634)[b]
Theophylline Sodium Glycinate elixir	USP (24, p. 1635)
Thiamine Hydrochloride elixir	USP (24, p. 1639)[b]
Thiamine Mononitrate elixir	USP (24, p. 1641)[b]

(Continued)

Dosage form	Reference
Thimerosal Topical aerosol	USP (24, p. 1644)[d]
Thimerosal tincture	USP (24, p. 1645)
Thiothixene Hydrochloride oral solution	USP (24, p. 1654)
Triprolidine Hydrochloride syrup	USP (24, p. 1717)
Powdered Valerian extract	USP (24), NF (19 First Suppl, p. 2729)

[a]Chromatographic conditions: Column–Glass 1.8 *m* × 4 mm I.D. S3 (100–120 mesh) or with S8
[d]Carrier Gas – Nitrogen or Helium; Temperature – 120°C; Detector–FID
[b]Internal Standard – Acetonitrile, Acetone
[c]Isopropyl Alcohol
[d]Methyl Ethyl Ketone

Table 9 Compendial applications of GC for the presence of organic volatile impurities in pharmaceutical raw materials and dosage forms

Material/dosage forms	Chapter ≤467≥	Reference
Acacia	Method I[b]	NF (19, p. 2408)
Acetaminophen	Method V[b]	USP (24, p. 17)
Acetazolamide	Method V	USP (24, p. 40)
Acetic Acid	Method IV[b]	NF (19, p. 2408)
Acetohexamide	Method V	USP (24, p. 42)
Acetohydroxamic Acid	Method I	USP (24, p.43)
Acetylcholine Chloride	Method I	USP (24, p. 44)
Acetylcysteine	Method I	USP (24, p. 45) and NF (19 p. 2409)
Acyclovir	Method V	USP (24, p. 46)
Adenine	Method V	USP (24, p. 50)
Agar	Method IV	NF (19, p. 2410)
Alanine	Method I	USP (24, p. 52)
Albuterol Sulfate	Method I	USP (24, p. 55)
Allopurinol	Method V	USP (24, p. 62)
Aluminium Monostearate	Method IV	NF (19, p. 2412)
Aluminium Sulfate	Method IV	USP (24, p. 91)
Amantadine Hydrochloride	Method I	USP (p. 103)
Amiloride Hydrochloride	Method V	USP (24, p. 107)
Aminoglutehimide	Method V	USP (24, p. 112)
Aminophylline	Method I	USP (24, p. 115
Amitriptyline Hydrochloride	Method I	USP (24, p. 122)
Amobarbital Sodium	Method I	USP (24, p. 126)
Amodiaquine Amodiaquine Hydrochloride	Method V	USP (24, pp. 126 and 127)
Amphetamine Sulfate	Method I	USP (24, p. 134)
Amyl Nitrate	Method V	USP (24, p. 145)
Amylene Hydrate	Method I	NF (19, p. 2414)
Anethole	Method V	NF (19, p. 2414)
Arginine	Method I	USP (24, p. 158) and NF (19, p. 2415)
Arginine Hydrochloride	Method I	USP (24, p. 158)
Aromatic Elixir	Method I	NF (19, p. 2415)
Ascorbic Acid	Method IVx	USP (24, p. 160) and NF (19, p. 2415)
Ascorbyl Palmitate	Method IV	NF (19, p. 2415)
Aspirin	Method IV	USP (24, p. 161)
Aspartame	Method IV	NF (19, p. 2415)
Atropine	Method V	USP (24, p. 177)
Atropine Sulfate	Method I	USP (24, p. 178)
Activated Attapulgite Colloidal Activated Attapulgite	Method IV	USP (24, p. 180)
Azathioprine	Method V	USP (24, p. 184)
Baclofen	Method IV	USP (24, p. 194)
Belladonna Extract	Method IV	USP (24, p. 199)
Bendroflumethiazide	Method V	USP (24, p. 201)
Bentonite Purified Bentonite Bentonite Magma	Method IV	NF (19, pp. 2416, 2417 and 2418)
Benzaldehyde	Method V	NF (19, p. 2418)
Compound Benzaldehyde Elixir	Method I	NF (19, p. 2419)
Benzonatate	Method I	USP (24, p. 211)
Benztropine Mesylate	Method I	USP (24, p. 213)
Benzyl Alcohol	Method V	NF (19, p. 2420)
Benzyl Benzoate	Method V	USP (24, p. 215) and NF (19, p. 2421)

(Continued)

(Continued)

Table 9 Compendial applications of GC for the presence of organic volatile impurities in pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage forms	Chapter ≤467≥	Reference
Beta Carotene	Method IV	USP (24, p. 216)
Betamethasone	Method V	USP (24, p. 217)
Bethanechol Chloride	Method I	USP (24, p. 229)
Biotin	Method V	USP (24, p. 234)
Biperiden Biperiden Hydrochloride	Method IV	USP (24, p. 234)
Bromocriptine Mesylate	Method V	USP (24, p. 248)
Bromodiphenhydramine Hydrochloride	Method I	USP (24, p. 251)
Brompheniramine Maleate	Method I	USP (24, p. 251)
Busulfan	Method V	USP (24, p. 260)
Butabarbital	Method V	USP (24, p. 261)
Butabarbital Sodium	Method I	USP (24, p. 261)
Butalbital	Method V	USP (24, p. 263)
Butylated Hydroxyanisole	Method V	NF (19, p. 2422)
Butylated Hydroxytoluene	Method IV	NF (19, p. 2423)
Butyl Paraben	Method IV	NF (19, p. 2423)
Caffeine	Method I	USP (24, p. 272)
Calcifediol	Method V	USP (24, p. 274)
Calcium Acetate	Method I	USP (24, p. 275)
Calcium Carbonate	Method IV	USP (24, p. 277) and NF (19, p. 2423)
Calcium Chloride	Method I	USP (24, p. 282) and NF (19, p. 2423)
Calcium Citrate	Method IV	USP (24, p. 282)
Calcium Gluceptate	Method I	USP (24, p. 283)
Calcium Gluconate	Method I	USP (24, p. 284)
Calcium Hydroxide	Method IV	USP (24, p. 286)
Calcium Lactate	Method I	USP (24, p. 287)
Calcium Lactobionate	Method I	USP (24, p. 288)
Calcium Levulinate	Method I	USP (24, p. 288)
Calcium Pantotothenate Racemic Calcium Pantothenate	Method I	USP (24, pp. 289 and 290)
Dibasic Calcium Phosphate	Method IV	USP (24, p. 290) and NF (19, p. 2423)
Calcium Polycarbophil	Method IV	USP (24, p. 291)
Calcium Saccharate	Method IV	USP (24, p. 291) and NF (19, p. 2424)
Calcium Stearate	Method IV	NF (19, p. 2425)
Captopril	Method I	USP (24, p. 296)
Carbamazepine	Method V	USP (24, p. 299)
Carbamide Peroxide	Method I	USP (24, p. 301)
Carbidopa	Method IV	USP (24, p. 304)
Carbinoxamine Maleate	Method I	USP (24, p. 305)
Carbomer 934P	Method IV	NF (19, p. 2427)
Carboxymethylcellulose Calcium	Method IV	NF (19, p. 2428)
Carboxymethylcellulose Sodium	Method IV	USP (24, p. 313) and NF (19, p. 2429)
Carboxymethylcellulose Sodium 12	Method IV	NF (19, p. 2429)
Carisoprodol	Method V	USP (24, p. 314)
Cellacefate	Method IV	NF (19, p. 2431)
Microcrystalline Cellulose	Method IV	NF (19, p. 2432)
Microcrytsalline Cellulose and Carboxymethylcellulose Sodium	Method IV	NF (19 p. 2433)
Powdered Cellulose	Method IV	NF (19, p. 2433)
Cellulose Acetate	Method IV	NF (19, p. 2434)
Cetylpyridium Chloride	Method V	USP (24, p. 370)
Chloral Hydrate	Method I	USP (24, p. 371)
Chlorambucil	Method V	USP (24, p. 372)
Chlordiazepoxide	Method IV	USP (24, pp. 381 and 384)
Chlordiazepoxide Hydrochloride		
Chlorobutanol	Method IV	NF (19, p. 2437)
Chloroquine	Method V	USP (24, p. 388)
Chloroquine Phosphate	Method I	USP (24, p. 389)
Chlorothiazide	Method V	USP (24, p. 389)
Chlorpheniramine Maleate	Method IV	USP (24, p. 392)
Chlorpromazine	Method V	USP (24, p. 395)
Chlorpromazine Hydrochloride	Method I	USP (24, p. 396)
Chlorpropamide	Method IV	USP (24, p. 398)
Chlorzoxazone	Method V	USP (24, p. 403)
Cholecalciferol	Method IV	USP (24, p. 404)
Cholesterol	Method IV	NF (19, p. 2438)
Cholestyramine Resin	Method IV	USP (24, p. 406)
Cimetidine	Method IV	USP (24, p. 412)
Cinoxacin	Method IV	USP (24, p. 415)
Citric Acid	Method IV	USP (24, p. 423) and NF (19, p. 2438)
Clidinium Bromide	Method I	USP (24, p. 429)
Clofibrate	Method V	USP (24, p. 442)
Clomiphene Citrate	Method V	USP (24, p. 444)
Clonazepam	Method V	USP (24, p. 445)
Clorazepate Dipotassium	Method I	USP (24, p. 448)
Cocoa Butter	Method IV	NF (19, p. 2438)

(Continued)

(Continued)

Table 9 Compendial applications of GC for the presence of organic volatile impurities in pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage forms	Chapter ≤467≥	Reference
Colchicine	Method I	USP (24, p. 464)
Corn Oil	Method IV	NF (19, p. 2439)
Cortisone Acetate	Method IV	USP (24, p. 473)
Cottonseed oil	Method IV	NF (19, p. 2439)
Cromolyn Sodium	Method I	USP (24, p. 475)
Croscarmellose Sodium	Method IV	NF (19, p. 2441)
Cupric Chloride	Method V	USP (24, p. 477)
Cupric Sulfate	Method IV	USP (24, p. 479)
Cyclizine Hydrochloride	Method IV	USP (24, p. 481)
Cyclobenzaprine Hydrochloride	Method I	USP (24, p. 481)
Cyproheptadine Hydrochloride	Method V	USP (24, p. 489)
Cysteine Hydrochloride	Method IV	USP (24, p. 490)
Danazol	Method V	USP (24, p. 495)
Dapsone	Method V	USP (24, p. 496)
Dehydrocholic Acid	Method V	USP (24, p. 500)
Desipramine	Method I	USP (24, p. 505)
Dexamethasone	Method IV	USP (24, p. 512)
Dexamethasone Acetate	Method V	USP (24, p. 515)
Dexamethasone Sodium Phosphate	Method IV	USP (24, p. 516)
Dexbrompheniramine Maleate	Method I	USP (24, p. 520)
Dexchlorpheniramine Maleate	Method I	USP (24, p. 521)
Dexpanthenol	Method IV	USP (24, p. 523)
Dextrates	Method I	NF (19, p. 2444)
Dextrin	Method I	NF (19, p. 2444)
Dextroamphetamine Sulfate	Method I	USP (24, p. 528)
Dextrose Excipient	Method I	NF (19, p. 2445)
Diazepam	Method V	USP (24, p. 538)
Dichlorphenamide	Method V	USP (24, p. 545)
Dicyclomine Hydrochloride	Method I	USP (24, p. 549)
Diethanolamine	Method IV	NF (19, p. 2446)
Diethylpropion Hydrochloride	Method I	USP (24, p. 552)
Diethylstilbestrol	Method V	USP (24, p. 554)
Diethylstilbestrol Diphosphate	Method V	USP (24, p. 555)
Diflunisal	Method V	USP (24, p. 558)
Digitalis Powdered Digitalis	Method IV	USP (24, p. 560)
Dihydrotachysterol	Method IV	USP (24, p. 568)
Dihydroxyaluminum Aminoacetate	Method IV	USP (24, p. 570)
Dihydroxyaluminum Sodium Carbonate	Method IV	USP (24, p. 572)
Diltiazem Hydrochloride	Method IV	USP (24, p. 573)
Dimenhydrinate	Method V	USP (24, p. 576)
Diphenhydramine Citrate	Method V	USP (24, p. 582)
Diphenhydramine Hydrochloride	Method I	USP (24, p. 583)
Dipyridamole	Method IV	USP (24, p. 590)
Disopyramide Phosphate	Method I	USP (24, p. 593)
Disulfiram	Method V	USP (24, p. 594)
Doxepin Hydrochloride	Method I	USP (24, p. 604)
Doxylamine Succinate	Method I	USP (24, p. 612)
Dyphylline	Method I	USP (24, p. 618)
Enalapril Maleate	Method IV	USP (24, p. 638)
Ephedrine Ephedrine Hydrochloride Ephedrine Sulfate	Method I	USP (24, pp. 642 and 643)
Ergocalciferol	Method V	USP (24, p. 651)
Conjugated Estrogens Esterified Estrogens	Method V	USP (24, pp. 681 and 683)
Estropipate	Method V	USP (24, p. 686)
Ethacrynic Acid	Method V	USP (24, p. 688)
Ethambutol Hydrochloride	Method I	USP (24, p. 689)
Ethionamide	Method V	USP (24, p. 694)
Ethosuximide	Method I	USP (24, p. 695)
Ethyl Acetate	Method I 30 $M \times 0.53$ mm I.D. fused Silica column with G16 (1 μm)	NF (19, p. 2450)
Ethyl Vanillin	Method IV	NF (19, p. 2450)
Ethylcellulose	Method IV	NF (19, p. 2451)
Ethylcellulose aqueous dispersion	Method V	NF (19, p. 2451)
Ethylparaben	Method IV	NF (19, p. 2452)
Ethylenediamine	Method V	USP (24, p. 698)
Ethynodiol Diacetate	Method IV	USP (24, p. 698)
Etidronate Disodium	Method I	USP (24, p. 700)
Eucatropine Hydrochloride	Method I	USP (24, p. 706)
Famotidine	Method V	USP (24, p. 707)
Fenoprofen Calcium	Method V	USP (24, p. 708)
Ferrous Fumurate	Method IV	USP (24, p. 7111)
Ferrous Gluconate	Method I	USP (24, p. 712)
Ferrous Sulfate Dried Ferrous Sulfate	Method IV	USP (24, p. 715)

(Continued)

(Continued)

Table 9 Compendial applications of GC for the presence of organic volatile impurities in pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage forms	Chapter ≤467≥	Reference
Flucytosine	Method V	USP (24, p. 719)
Fluoxetine Hydrochloride	Method IV	USP (24, p. 738)
Fluoxymesterone	Method V	USP (24, p. 740)
Fluphenazine Hydrochloride	Method I	USP (24, p. 743)
Flurazepam Hydrochloride	Method I	USP (24, p. 746)
Flurbiprofen Sodium	Method I	USP (24, p. 749)
Folic Assay	Method IV	USP (24, p. 752)
Fumaric Acid	Method V	NF (19, p. 2453)
Furosemide	Method V	USP (24, p. 756)
Galageenan	Method IV	NF (19, p. 2454)
Gemfibrozil	Method V	USP (24, p. 763)
Liquid Glucose	Method I	NF (19, p. 2461)
Glyceryl Behenate	Method IV	NF (19, p. 2462)
Glyceryl Monostearate	Method IV	NF (19, p. 2463)
Glycine	Method I	USP (24, p. 782) and NF (19, p. 2464)
Griseofulvin	Method V	USP (24, p. 788)
Guaifenesin	Method IV	USP (24, p. 791)
Guar gum	Method IV	NF (19, p. 2464)
Guanabenz Acetate	Method V	USP (24, p. 796)
Guanadrel Sulfate	Method I	USP (24, p. 797)
Guanethidine Monosulfate	Method I	USP (24, p. 799)
Haloperidol	Method V	USP (24, p. 804)
Homatropine Methylbromide	Method I	USP (24, p. 815)
Hydralazine Hydrochloride	Method I	USP (24, p. 818)
Hydrochlorothiazide	Method V	USP (24, p. 820)
Hydrocodone Bitartrate	Method I	USP (24, p. 821)
Hydrocortisone	Method IV	USP (24, p. 824)
Hydrocortisone Sodium Phosphate	Method I	USP (24, p. 831)
Hydroflumethiazide	Method V	USP (24, p. 835)
Hydromorphone Hydrochloride	Method I	USP (24, p. 836)
Hydroquinone	Method I	USP (24, p. 838)
Hydroxychloroquine Sulfate	Method I	USP (24, p. 841)
Hydroxyethyl Cellulose	Method IV	NF (19, p. 2465)
Hydroxypropyl Cellulose	Method IV	NF (19, p. 2465)
Hydroxypropyl Methylcellulose	Method IV	USP (24, p. 843) and NF (19, p. 2466)
Hydroxyurea	Method I	USP (24, p. 844)
Hydroxyzine Hydrochloride	Method I	USP (24, p. 846)
Hydroxyzine Pamoate	Method V	USP (24, p. 848)
Hypromellose Phthalate	Method IV	NF (19, p. 2467)
Hyoscyamine Sulfate	Method I	USP (24, p. 851)
Ibuprofen	Method V	USP (24, p. 854)
Imidurea	Method I	NF (19, p. 2467)
Imipramine Hydrochloride	Method I	USP (24, p. 865)
Indapamide	Method IV	USP (24, p. 867)
Indomethacin	Method IV	USP (24, p. 874)
Iopromide	Method IV	USP (24, p. 904)
Isoleucine	Method I	USP (24, p. 923)
Isoniazid	Method I	USP (24, p. 924)
Isopropamide Iodide	Method I	USP (24, p. 926)
Isopropyl Myristate	Method IV	NF (19, p. 2468)
Isopropyl Palmitate	Method IV	NF (19, p. 2468)
Isoproterenol Hydrochloride	Method I	USP (24, p. 928)
Isoproterenol Sulfate	Method I	USP (24, p. 932)
Isotretinon	Method V	USP (24, p. 938)
Isoxsuprine Hydrochloride	Method V	USP (24, p. 940)
Ketoconazole	Method IV	USP (24, p. 945)
Ketoprofen	Method IV	USP (24, p. 946)
Ketorolac Tromethamine	Method V	USP (24, p. 947)
Labetalol Hydrochloride	Method I	USP (24, p. 949)
Lactitol	Method IV	NF (19, p. 2469)
Lecithin	Method IV	NF (19, p. 2471)
Levmetamfetamine	Method I	USP (24, p. 959)
Levodopa	Method IV	USP (24, p. 963)
Lime	Method IV	USP (24, p. 974)
Lithium Carbonate	Method I	USP (24, p. 981)
Lithium Citrate	Method V	USP (24, p. 983)
Lithium Hydroxide	Method V	USP (24, p. 984)
Loxapine Succinate	Method V	USP (24, p. 993)
Lysine Acetate	Method I	USP (24, p. 994)
Lysine Hydrochloride	Method I	USP (24, p. 994)
Mafenide Acetate	Method V	USP (24, p. 995)
Magaldrate	Method V	USP (24, p. 996)
Magnesium Chloride	Method I	USP (24, p. 1002)
Magnesium Citrate	Method IV	USP (24, p. 1003)
Magnesium Gluconate	Method I	USP (24, p. 1004)
Magnesium Salicylate	Method I	USP (24, p. 1008)
Magnesium Silicate	Method IV	NF (19, p. 2473)
Magnesium Stearate	Method IV	NF (19, p. 2473)
Magnesium Sulfate	Method I	USP (24, p. 1009)
Malic Acid	Method I	NF (19, p. 2475)
Mandelic Acid	Method IV	USP (24, p. 1012)
Manganese Chloride	Method I	USP (24, p. 1012)
Manganese Gluconate	Method I	USP (24, p. 1013)

(Continued)

(Continued)

Table 9 Compendial applications of GC for the presence of organic volatile impurities in pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage forms	Chapter ≤467≥	Reference
Manganese Sulfate	Method I	USP (24, p. 1014)
Maprotiline Hydrochloride	Method V	USP (24, p. 1016)
Mecamylamine Hydrochloride	Method I	USP (24, p. 1023)
Meclizine Hydrochloride	Method IV	USP (24, p. 1025)
Meclofenamate Sodium	Method I	USP (24, p. 1027)
Megestrol Acetate	Method IV	USP (24, p. 1030)
Melphalan	Method IV	USP (24, p. 1032)
Menthol	Method V	USP (24, p. 1038)
Meperidine Hydrochloride	Method I	USP (24, p. 1039)
Mephenytoin	Method V	USP (24 - NF 19) First Suppl, (p. 2639)
Meprobamate	Method V	USP (24, p. 1043)
Mercaptopurine	Method V	USP (24, p. 1044)
Mesoridazine Besylate	Method I	USP (24, p. 1048)
Metaproterenol Sulfate	Method IV	USP (24, p. 1051)
Methacrylic Acid copolymer	Method V	NF (19, p. 2477)
Methadone Hydrochloride	Method I	USP (24, p. 1056)
Methamphetamine Hydrochloride	Method I	USP (24, p. 1058)
Methazolamide	Method I	USP (24, p. 1060)
Methdilazine Hydrochloride	Method I	USP (24, p. 1061)
Methenamine Methenamine Hippurate Methenamine Mandelate	Method I	USP (24, pp. 1062, 1063 and 1064)
Methimazole	Method I	USP (24, p. 1066)
Methionine	Method I	USP (24, p. 1067)
Methocarbamol	Method V	USP (24, p. 1067)
Methotrexate	Method V	USP (24, p. 1070)
Methoxsalen	Method V	USP (24, p. 1073)
Methsuximide	Method V	USP (24, p. 1075)
Methyl Salicylate	Method IV	NF (19, p. 2479)
Methylcellulose	Method V	USP (24, p.1079) and NF (19, p. 2480)
Methyldopa	Method V	USP (24, p.1080)
Methylene Blue	Method I	USP (24, p.1085)
Methylene Chloride in coated tablets	Method V	USP (24, p.1878)
Methylparaben	Method IV	NF (19, p. 2480)
Methylparaben Sodium	Method I	NF (19, p. 2481)
Methylphenidate Hydrochloride	Method I	USP (24, p. 1088)
Methyltestosterone	Method V	USP (24, p. 1094)
Metoclopramide Hydrochloride	Method I	USP (24, p. 1097)
Metoprolol Fumarate	Method I	USP (24, p. 1100)
Metoprolol Tartrate	Method I	USP (24, p. 1101)
Metyrosine	Method IV	USP (24, p. 1108)
Mexiletine Hydrochloride	Method I	USP (24, p. 1109)
Minoxidil	Method IV	USP (24, p. 1118)
Mititane	Method V	USP (24, p. 1120)
Monoethanolamine	Method I	NF (19, p. 2484)
Monosodium Glutamate	Method I	NF (19, p. 2484)
Monothioglycerol	Method IV	NF (19, p. 2484)
Moricizine Hydrochloride	Method V	USP (24, p. 1129)
Morphine Sulfate	Method I	USP (24, p. 1131)
Nadolol	Method IV	USP (24, p. 1134)
Nandrolone Decanoate	Method V	USP (24, p. 1144)
Nandrolone Phenpropionate	Method V	USP (24, p. 1145)
Naproxen	Method V	USP (24, p. 1147)
Naproxen Sodium	Method I	USP (24, p. 1149)
Niacin	Method IV	USP (24, p. 1176)
Niacinamide	Method I	USP (24, p. 1179)
Nifedipine	Method V	USP (24, p. 1183)
Norethindrone	Method IV	USP (24, p. 1196)
Norethindrone Acetate	Method IV	USP (24, p. 1199)
Norethynodrel	Method V	USP (24, p. 1202)
Nortriptyline Hydrochloride	Method I	USP (24, p. 1206)
Octoxynol	Method IV	NF (19, p. 2486)
Octyldodecanol	Method V	NF (19, p. 2486)
Oleic Acid	Method IV	NF (19, p. 2486)
Oleovitamin A and D	Method V	USP (24, p. 1217)
Olive Oil	Method IV	NF (19, p. 2487)
Omeprazole	Method IV	USP (24, p. 1217)
Oxandrolone	Method V	USP (24, p. 1225)
Oxazepam	Method V	USP (24, p. 1226)
Oxprenolol Hydrochloride	Method I	USP (24, p. 1228)
Oxtriphylline	Method I	USP (24, p. 1229)
Oxybutynin Chloride	Method I	USP (24, p. 1232)
Oxymetholone	Method V	USP (24, p. 1242)
Oxyquinoline Sulfate	Method I	NF (19, p. 2487)
Panthenol	Method I	USP (24, p. 1258)
Papaverine Hydrochloride	Method IV	USP (24, p. 1260)
Peanut Oil	Method IV	NF (19, p. 2488)
Pectin	Method IV	USP (24, p. 1265) and NF (19, p. 2489)
Pentobarbital	Method V	USP (24, p. 1293)
Pentobarbital Sodium	Method I	USP (24, p. 1294)
Peppermint	Method IV	NF (19, p. 2489)

(Continued)

(Continued)

Table 9 Compendial applications of GC for the presence of organic volatile impurities in pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage forms	Chapter ≤467≥	Reference
Peppermint water	Method I	NF (19, p. 2490)
Perphenazine	Method V	USP (24, p. 1296)
Phendimetrazine Tartrate	Method I	USP (24, p. 1301)
Phenelzine Sulfate	Method I	USP (24, p. 1303)
Pheniramine Maleate	Method IV	USP (24, p. 1304)
Phenmetrazine Hydrochloride	Method I	USP (24, p. 1304)
Phenobarbital	Method V	USP (24, p. 1305)
Phenobarbital Sodium	Method I	USP (24, p. 1307)
Phenol Liquefied Phenol	Method I	USP (24, p. 1308)
Phenoxybenzamine Hydrochloride	Method V	USP (24, p. 1308)
Phensuximide	Method V	USP (24, p. 1309)
Phentermine Hydrochloride	Method I	USP (24, p. 1310)
Phenylalanine	Method I	USP (24, p. 1313)
Phenylbutazone	Method V	USP (24, p. 1313)
Phenylethyl Alcohol	Method IV	USP (24, p. 1318) and NF (19, p. 2490)
Phenylmercuric Acetate	Method IV	NF (19, p. 2490)
Phenylmercuric Nitrate	Method IV	NF (19, p. 2490)
Phenylpropanolamine Bitartrate Phenylpropanolamine Hydrochloride	Method I	USP (24, pp. 1318 and 1319)
Phenytoin Phenytoin Sodium	Method V	USP (24, pp. 1322 and 1324)
Pimozide	Method V	USP (24, p. 1335)
Pindolol	Method V	USP (24, p. 1336)
Piroxicam	Method V	USP (24, p. 1342)
Polacrilin Potassium	Method IV	NF (19, p. 2492)
Polycarbophil	Method IV	USP (24, p. 1348)
Poloxamer	Method V	NF (19, p. 2492)
Polyethylene Glycol	Method IV	NF (19, p. 2493)
Polyethylene Oxide	Method I	NF (19, p. 2497)
Polyoxyl 10 Oleyl Ether	Method V	NF (19, p. 2498)
Polyoxyl 20 Cetostearyl Ether	Method I	NF (19, p. 2499)
Polyoxyl 35 Castor oil	Method I	NF (19, p. 2500)
Polyoxyl 40 Hydrogenated Castor oil	Method I	NF (19, p. 2501)
Polyoxyl 40 Stearate	Method I	NF (19, p. 2501)
Polysorbate 20 Polysorbate 40 Polysorbate 60 Polysorbate 80	Method IV	NF (19, pp. 2501 and 2502)
Polyvinyl Acetate Phthalate	Method IV	NF (19, p. 2502)
Polyvinyl Alcohol	Method I	USP (24, p. 1352) and NF (19, p. 2503)
Sulfurated Potash	Method IV	USP (24, p. 1353)
Potassium Benzoate	Method I	NF (19, p. 2503)
Potassium Bicarbonate	Method IV	USP (24, p. 1354)
Potassium Carbonate	Method I	USP (24, p. 1357) and NF (19, p. 2503)
Potassium Chloride	Method I	USP (24, p. 1357) and NF (19, p. 2503)
Potassium Citrate	Method I	USP (24, p. 1362) and NF (19, p. 2503)
Potassium Gluconate	Method I	USP (24, p. 1364)
Potassium Iodide	Method I	USP (24, p. 1368)
Potasium Metabisulfite	Method V	NF (19, p. 2503)
Potassium Perchlorate	Method I	USP (24, p. 1370)
Monobasic Potassium Phosphate	Method I	NF (19, p. 2504)
Potassium Sorbate	Method I	NF (19, p. 2504)
Prazosin Hydrochloride	Method IV	USP (24, p. 1379)
Primaquine Phosphate	Method I	USP (24, p. 1391)
Primidone	Method V	USP (24, p. 1392)
Probenecid	Method V	USP (24, p. 1393)
Probucol	Method V	USP (24, p. 1395)
Procainamide Hydrochloride	Method I	USP (24, p. 1397)
Procarbazine Hydrochloride	Method I	USP (24, p. 1403)
Prochlorperazine Edisylate	Method I	USP (24, p. 1405)
Prochlorperazine Maleate	Method V	USP (24, p. 1406)
Procyclidine Hydrochloirde	Method V	USP (24, p. 1406)
Proline	Method I	USP (24, p. 1409)
Promazine Hydrochloride	Method I	USP (24, p. 1410)
Propantheline Bromide	Method I	USP (24, p. 1415)
Propionic Acid	Method I	NF (19, p. 2505)
Propoxyphene Hydrochloride	Method I	USP (24, p. 1420)
Propoxyphene Napsylate	Method V	USP (24, p. 1424)
Propranolol Hydrochloride	Method I	USP (24, p. 1428)
Propyl Gallate	Method V	NF (19, p. 2506)
Propylene Carbonate	Method I	NF (19, p. 2506)

(Continued)

(Continued)

Table 9 Compendial applications of GC for the presence of organic volatile impurities in pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage forms	Chapter ≤467≥	Reference
Propylene Glycol	Method IV	USP (24, p. 1434) and NF (19, p. 2506)
Propylene Glycol Monostearate	Method IV	NF (19, p. 2507)
Propylparaben	Method IV	NF (19, p. 2508)
Propylparaben sodium	Method I	NF (19, p. 2508)
Propylthiouracil	Method V	USP (24, p. 1436)
Protriptyline Hydrochloride	Method I	USP (24, p. 1439)
Pseudoephedrine Hydrochloride	Method V	USP (24, p. 1439)
Pyrazinamide	Method I	USP (24, p. 1444)
Pyridostigmine Bromide	Method I	USP (24, p. 1446)
Pyridoxine Hydrochloride	Method I	USP (24, p. 1447)
Pyrilamine Maleate	Method I	USP (24, p. 1449)
Pyrimethamine	Method V	USP (24, p. 1450)
Pyroxylin	Method V	USP (24, p. 1451)
Quinidine Gluconate	Method I	USP (24,
Quinidine Sulfate		pp. 1453 and 1456)
Quinine Sulfate	Method IV	USP (24, p. 1458)
Racepinephrine	Method V	USP (24, p. 1461)
Racepinephrine Hydrochloride	Method I	USP (24, p. 1462)
Ranitidine Htdrochloride	Method I	USP (24, p. 1462)
Rauwolfia Serpentina	Method IV	USP (24, p. 1466)
Resorcinol	Method IV	USP (24, p. 1478)
Resorcinol Monoacetate	Method I	USP (24, p. 1479)
Riboflavin	Method IV	USP (24, p. 1480)
Riboflavin 5′-Phosphate Sodium	Method IV	USP (24, p. 1482)
Rimexolone	Method V	USP (24, p. 1487)
Ritodrine Hydrochloride	Method I	USP (24, p. 1493)
Strong Rose water	Method I	NF (19, p. 2508)
Saccharin	Method V	NF (19, p. 2509)
Saccharin Calcium	Method I	USP (24, p. 1497) and NF (19, p. 2509)
Saccharin Sodium	Method IV	USP (24, p. 1498)
Salicylamide	Method V	USP (24, p. 1499)
Salsalate	Method V	USP (24, p. 1502)
Scopalamine Hydrobromide	Method I	USP (24, p. 1507)
Secobarbital	Method V	USP (24, p. 1509)
Secobarbital Sodium	Method I	USP (24, p. 1510)
Selenious Acid	Method I	USP (24, p. 1514)
Serine	Method I	USP (24, p. 1517)
Sesame oil	Method IV	NF (19, p. 2512)
Silicon Dioxide Colloidal Silicon Dioxide	Method IV	NF (19, p. 2514)
Simethicone	Method IV	USP (24, p. 1518) and NF (19, p. 2515)
Sodium Acetate	Method IV	USP (24, p. 1524)
Sodium Ascorbate	Method I	USP (24, p. 1525) and NF (19, p. 2515)
Sodium Benzoate	Method IV	NF (19, p. 2516)
Sodium Bicarbonate	Method IV	USP (24, p. 1525) and NF (19, p. 2516)
Sodium Borate	Method I	NF (19, p. 2516)
Sodium Butyrate	Method I	USP (24 - NF 19) First Suppl (p. 2657)
Sodium Carbonate	Method I	NF (19, p. 2516)
Sodium Dehydroacetate	Method I	NF (19, p. 2516)
Sodium Fluoride	Method I	USP (24, p. 1532)
Sodium Formaldehyde Sulfoxylate	Method I	NF (19, p. 2517)
Sodium Iodide	Method I	USP (24, p. 1535)
Sodium Lauryl Sulfate	Method IV	NF (19, p. 2517)
Sodium Monofluorophosphate	Method I	USP (24, p. 1536)
Monobasic Sodium Phosphate	Method I	USP (24, p. 1540) and NF (19, p. 2518)
Sodium Propionate	Method I	NF (19, p. 2518)
Sodium Salicylate	Method I	USP (24, p. 1542)
Sodium Stearate	Method I	NF (19, p. 2519)
Sodium Stearyl Fumurate	Method IV	NF (19, p. 2519)
Sorbic Acid	Method IV	NF (19, p. 2520)
Sorbitan Monolaurate	Method V	NF (19, p. 2520)
Sorbitan Monooleate	Method IV	NF (19, p. 2521)
Sorbitan Monopalmitate	Method IV	NF (19, p. 2521)
Sorbitan Monostearate	Method IV	NF (19, p. 2522)
Sorbitol	Method IV	NF (19, p. 2522)
Spironolactone	Method V	USP (24, p. 1546)
Stanozolol	Method V	USP (24, p. 1549)
Starch Pregelatinized starch	Method IV	NF (19, pp. 2524 and 2525)
Stearic Acid Purified Stearic Acid	Method V	NF (19, p. 2525)
Storax	Method IV	USP (24, p. 1551)
Sucrose	Method IV	NF (19, p. 2527)
Compressible Sugar	Method 1V	NF (19, pp. 2528
Confectioner's Sugar		and 2529)
Sugar spheres		

(Continued)

(Continued)

Table 9 Compendial applications of GC for the presence of organic volatile impurities in pharmaceutical raw materials and dosage forms (*Continued*)

Material/dosage forms	Chapter ≤467≥	Reference
Sulfamethoxazole	Method IV	USP (24, p. 1571)
Sulfapyridine	Method V	USP (24, p. 1575)
Sulfasalazine	Method V	USP (24, p. 1576)
Sulfinpyrazone	Method V	USP (24, p. 1578)
Sulfisoxazole Acetyl	Method IV	USP (24, p. 1580)
Sulindac	Method V	USP (24, p. 1581)
Syrup	Method I	NF (19, p. 2530)
Tamoxifen Citrate	Method V	USP (24, p. 1586)
Tannic Acid	Method I	USP (24, p. 1588)
Tartaric Acid	Method I	NF (19, p. 2530)
Terbutaline Sulfate	Method I	USP (24, p. 1604)
Testolactone	Method V	USP (24, p. 1608)
Testosterone	Method V	USP (24, p. 1610)
Testosterone Cypionate	Method V	USP (24, p. 1610)
Testosterone Enanthate	Method V	USP (24, p. 1611)
Testosterone Propionate	Method IV	USP (24, p. 1612)
Theophylline	Method V	USP (24, p. 1628)
Theophylline Sodium Glycinate	Method I	USP (24, p. 1635)
Thiamine Hdrochloride	Method IV	USP (24, p. 1639)
Thiamine Mononitrate	Method IV	USP (24, p. 1641)
Thiethylperazine Maleate	Method V	USP (24, p. 1642)
Thioguanine	Method V	USP (24, p. 1646)
Thioridazine	Method V	USP (24, p. 1648)
Thioridazine Hydrochloride	Method IV	USP (24, p. 1649)
Thiothixene	Method V	USP (24, p. 1651)
Thiothixene Hydrochloride	Method I	USP (24, p. 1653)
Threonine	Method V	USP (24, p. 1654)
Thymol	Method IV	NF (19, p. 2530)
Tmolol Maleate	Method I	USP (24, p. 1663)
Titanium Dioxide	Method IV	USP (24, p. 1666)
Tocainide Hydrochloride	Method I	USP (24, p. 1672)
Tocopherols excipient	Method IV	NF (19, p. 2531)
Tolazamide	Method V	USP (24, p. 1674)
Tolbutamide	Method IV	USP (24, p. 1676)
Tolmetin Sodium	Method I	USP (24, p. 1677)
Tragacanth	Method IV	NF (19, p. 2531)
Trenbolone Acetate	Method IV	USP (24, p. 1683)
Triamterine	Method IV	USP (24, p. 1692)
Trientine Hydrochloride	Method I	USP (24, p. 1701)
Trifluoperazine Hydrochloride	Method I	USP (24, p. 1703)
Triflupromazine	Method V	USP (24, p. 1704)
Triflupromazine Hydrochloride	Method I	USP (24, p. 1705)
Trihexyphenidyl Hydrochloride	Method IV	USP (24, p. 1707)
Trioxsalen	Method V	USP (24, p. 1715)
Tripelennamine Hydrochloride	Method I	USP (24, p. 1716)
Triprolidine Hydrochloride	Method V	USP (24, p. 1716)
Trolamine	Method I	NF (19, p. 2533)
Tromethamine	Method V	USP (24, p. 1721) and NF (19, p. 2533)
Tryptophan	Method IV	USP (24, p. 1724)
Tyloxapol	Method I	USP (24, p. 1727) and NF (19, p. 2533)
Tyrosine	Method IV	USP (24, p. 1728)
Valine	Method I	USP (24, p. 1732)
Valproic Acid	Method V	USP (24, p. 1732)
Vanillin	Method IV	NF (19, p. 2534)
Hydrogenated vegetable oil	Method IV	NF (19, p. 2534)
Verapamil Hydrochloride	Method V	USP (24, p. 1739)
Vitamin E	Method IV	USP (24, p. 1747)
Vitamin E Polyethylene Glycol Succinate	Method I	NF (19, p. 2535)
Warfarin Sodium	Method I	USP (24, p. 1750)
Powdered Valerain extract	Method 1	USP (24 - NF 19) First Suppl, (p. 2728)
Carnauba wax	Method IV	NF (19, p. 2536)
Microcrystalline wax	Method IV	NF (19, p. 2536)
Xanthan gum	Method IV	NF (19, p. 2537)
Xylitol	Method I	NF (19, p. 2538)
Xylose	Method 1	USP (24, p. 1760) and NF (19, p. 2539)
Zein	Method IV	NF (19, p. 2539)
Zidovudine	Method V	USP (24, p. 1763)
Zinc Acetate	Method I	USP (24, p. 1766)
Zinc Chloride	Method I	USP (24, p. 1766)
Zinc Gluconate	Method I	USP (24, p. 1767)
Zinc Stearate	Method IV	USP (24, p. 1769)

(Continued)

Table 10 Chromatographic conditions for different methods

	Method I	Method IV	Method V	Method VI
Analytes	Benzene, Chloroform, 1,4-Dioxane, Methylene Chloride, Trichloroethylene	Benzene, Chloroform, 1,4-Dioxane, Methylene Chloride, Trichloroethylene	Benzene, Chloroform, 1,4-Dioxane, Methylene Chloride, Trichloroethylene	Benzene, Chloroform, 1,4-Dioxane, Methylene Chloride, Trichloroethylene
Column	30 *M* × 0.53 mm I.D. fused Silica analytical column with G27(5 μm) and a 5 *M* × 0.53 mm I.D. guard column deactivated with Phenylmethyl Siloxane	30 *M* × 0.53 mm I.D. fused Silica analytical column with G43 (3.0 μm) and a 5 *M* × 0.53 mm I.D. guard column deactivated with Phenylmethyl Siloxane	30 *M* × 0.53 mm I.D. fused Silica analytical column with G43 (3.0 μm) and a 5 *M* × 0.53 mm I.D. guard column deactivated with Phenylmethyl Siloxane	A: 2 *M* × 3 mm I.D. S3: temperature: 190°C B: 2.1 *M* × 3 mm I.D. S2: temperature: 160°C C: 30 *M* × 0.53 mm I.D. G16: temperature: 40°C D: 2 *M* × 3 mm I.D. G39: temperature: 65°C E: 2 *M* × 3 mm I.D. G16: temperature: 70°C F: 2.5 *M* × 2 mm I.D. S4: temperature: 120°C–200°C(2°C/min) H: 2.5 *M* × 2 mm I.D. G14: temperature: 45°C–120°C(8°C/min) I: 30 *M* × 0.53 mm I.D. G27: temperature: 35°C–175°C (8°C/min) 175°C - 260°C (35°C/min) J: 30 *M* × 0.33 mm I.D. G16: temperature: 50°C–165°C(6°C/min)
Carrier gas	Helium or Nitrogen	Helium	Helium	As appropriate for the column dimensions and temperature
Temperature (°C)	35–175 (8/min),175–260 (35/min)	40–240 (Rapidly)	40–240 (Rapidly)	
Detector	FID	FID	FID	FID
Internal	None	None	None	None
Standard procedure	Inject 1 μl	Inject using a heated gas-tight syringe, 1mL of headspace	Inject 1 μl	Inject 1 μl

Table 11 Miscellaneous compendial applications of GC for pharmaceutcial raw materials and dosage forms

Material/dosage form	Column	Carrier gas	Temp (°C)	Detector	Internal standard	Reference
Cocoa butter (fatty acid composition)	15 *M* × 0.25 mm fused Silica capillary with G 19 (0.25 μm)	Helium	180–240 10/min	FID	None	NF (19, p. 2438)
Corn oil (fatty acid composition)	Glass, 1.8 M × 4 mm I.D. 10% liquid G 4/S1A	Nitrogen	175	FID	None	NF (19, p. 2439)
Dexchlorpheniramine Maleate tablets (dissolution rate)	1.8 M × 2 mm I.D. 1.2% G16, 0.5% KOH/S1AB	Helium	205	FID	Dexbrompheniramine Maleate	USP (24, p. 522)
Fatty acid composition	30 M × 0.53 mm I.D. Fused Silica with G16 (1 μm)	Helium	70–260 5/min	FID	None	USP (24, p. 1871)
Mecamylamine Hydrochloride tablets (dissolution rate)	30 M × 0.53 mm I.D. capillary coated with G 27 (1–5 μm)	Helium	150	FID	Biphenyl	USP (24, p. 1023)
Organophosphorous insecticides (See Table 5 USP (24 Page 1890)	30 M × 0.53 mm I.D. fused Silica with G1 (0.25 μm)	Hydrogen, Helium or Nitrogen	80–150 30 /min 150–280 4/min	Alkali Fid or FPD	None	USP (24, p. 1889)
Organochlorine and Pyrethroid insecticides (See Table 6 USP 24 Page 1890)	30 M × 0.32 mm I.D. fused Silica with G1 (0.25 μm)	Hydrogen, Helium or Nitrogen	80–150 30/min 150–280 4/min	ECD	None	USP (24, p. 1890)
Saw Palmetto (fatty acid content) Powdered Saw Palmetto (fatty acid content)	30 M × 0.25 mm I.D. fused Silica capillary with G16(0.25 μm)	Helium	120–220 50/min	FID	Nonadecane	NF 19, pp. 2510 and 2512)
Safflower oil (fatty acid composition)	Glass, 1.5 M × 4 mm I.D. 10% liquid G4/S1A	Nitrogen	175	FID	None	USP (24, p. 1499)
Soybean Oil (fatty acid composition)	Glass, 1.5 M × 4 mm I.D. 10% liquid G4/S1A	Nitrogen	175	FID	None	USP (24, p. 1544 and NF 19, p. 2524)

USP 24 NF-19 2000 (21)

Phases

G1 Dimethylpolysiloxane oil
G2 Dimethylpolysiloxane gum
G3 50% Phenyl-50% methylpolysiloxane
G4 Diethylene glycol succinate polyester
G5 3-Cyanopropylpolysiloxane
G6 Trifluoropropylmethylpolysiloxane
G7 50% 3-Cyanopropyl-50% phenylmethylsilicone
G8 90% 3-Cyanopropyl-10% phenylmethylsilicone
G9 Methylvinylpolysiloxane
G10 Polyamide formed by reacting a C_{36} dicarboxylic acid with 1,3-di-4-piperdylpropane and piperidine in the respective mole ratios of 1.00:0.90:0.20
G11 *Bis*(2-ethylhexyl) sebacate polyester
G12 Phenyldiethanolamine succinate polyester
G13 Sorbitol
G14 Polyethylene glycol (average molecular weight of 950–1050)
G15 Polyethylene glycol (average molecular weight of 3000–3700)
G16 Polyethylene glycol compound (average molecular weight about 15,000). A high-molecular-weight compound of polyethylene glycol with a diepoxide linker. Available commercially as polyethylene glycol compound 20M, or as Carbowax 20M, from suppliers of chromatographic reagents.
G17 75% Phenyl-25% methylpolysiloxane
G18 Polyalkylene glycol
G19 25% Phenyl–25% cyanopropyl-50% methylsilicone
G20 Polyethylene glycol (average molecular weight of 380–420)
G21 Neopentyl glycol succinate

G22 *Bis*(2-ethylhexyl) phthalate
G23 Polyethylene glycol adipate
G24 Diisodecyl phthalate
G25 Polyethylene glycol compound TPA. A high-molecular-weight compound of a polyethylene glycol and a diepoxide that is esterified with terephthalic acid. Available commercially as Carbowax 20M-TPA from suppliers of chromatographic reagents.
G26 25% 2-Cyanoethyl-75% methylpolysolixane
G27 5% Phenyl-95% methylpolysiloxane
G28 25% Phenyl-75% methylpolysiloxane
G29 3-3′-Thiodipropionitrile
G30 Tetraethylene glycol dimethyl ether
G31 Nonylphenoxypoly(ethyleneoxy)ethanol (average ethyleneoxy chain length is 30); Nonoxynol 30
G32 20% Phenylmethyl-80% dimethylpolysiloxane
G33 20% Carborane–80% methylsilicone
G34 Diethylene glycol succinate polyester stabilized with phosphoric acid
G35 A high molecular weight compound of a polyethylene glycol and a diepoxide that is esterified with nitroterephthalic acid
G36 1% Vinyl–5% phenylmethylpolysiloxane
G37 Polyimide
G38 Phase G1 containing a small percentage of tailing inhibitor (Commercially available as SP2100/0.1% Carbowax 1500 from Supelco)
G39 Polyethylene glycol (average molecular weight about 1500)
G40 Ethylene glycol adipate
G41 Phenylmethyldimethylsilicone (10% phenyl-substituted)
G42 35% phenyl–65% dimethylpolysiloxane (percentages refer to molar substitution)
G43 6% cyanopropylphenyl–94% dimethylpolysiloxane (percentages refer to molar substitution)
G44 2% low-molecular-weight petrolatum hydrocarbon grease and 1% solution of potassium hydroxide
G45 Divinylbenzene-ethylene glycol-dimethylacrylate
G46 14% cyanopropylphenol–86% methylpolysiloxane

Supports *USP 24 NF-19 2000 (21) (NOTE: Unless otherwise specified, mesh sizes of 80–100 or, alternatively, 100–120 are intended.)*

S1A Siliceous earth for gas chromatography has been flux calcined by mixing diatomite with Na_2CO_3 flux and calcining above 900°. The siliceous earth is acid-washed, then water-washed until neutral, but not base-washed. The siliceous earth may be silanized by treating with an agent such as dimethyldichlorosilane (unless otherwise specified in the individual monograph, silanized support is intended) to mask surface silanol groups.
S1AB The siliceous earth as described above is both acid- and base-washed (unless otherwise specified in the individual monograph, silanized support is intended).
S1C A support prepared from crushed firebrick and calcined or burned with a clay binder above 900° with subsequent acid-wash. It may be silanized.
S1NS The siliceous earth is untreated.
S2 Styrene–divinylbenzene copolymer having a nominal surface area of less than 50 m^2 per g and an average pore diameter of 0.3–0.4 μm.
S3 Copolymer of ethylvinylbenzene and divinylbenzene, having a nominal surface area of 500–600 m^2/g and an average pore diameter of 0.0075 μm.
S4 tyrene-divinylbenzene copolymer with aromatic -O and -N groups, having a nominal surface area of 400–600 m^2/g and an average pore diameter of 0.0076 μm.
S5 40- to 60 mesh, high molecular weight tetrafluorethylene polymer.
S6 Styrene–divinylbenzene copolymer, having a nominal surface area of 250–350 m^2/g and an average pore diameter of 0.0091μm.
S7 Graphitized carbon having a nominal surface area of 12 m^2/g.
S8 Copolymer of 4-vinyl-pyridine and styrene–divinylbenzene.
S9 A porous polymer based on 2,6-diphenyl-p-phenylene oxide.
S10 A highly polar cross-linked copolymer of acrylonitrite and divinylbenzene.
S11 Graphitized carbon having a nominal surface area of 9 m^2/g modified with small amounts of petrolatum and polyethylene glycol compound (commercially available as SP1500 on Carbopack B from Supelco).
S12 Graphitized carbon having a nominal surface area of 100 m^2/g.

Biological Fluids

While it is clearly apparent that packed columns are mainly used for the various compendial tests, the use of capillary columns for the determination of therapeutic agents in biological fluids has become increasingly

popular. The high resolution capability of capillary columns often overcomes the problems of interference from the biological sample matrix and, coupled with specificity and increased sensitivity has made possible the quantitative analysis of many, formerly undeterminable drugs in biological fluids. In particular, drugs with very poor ultraviolet (UV) molar absorptivities, as well as drugs which by virtue of their specific physicochemical properties result in extremely low recovery values when extracted from biological fluids, have been successfully determined by GC using capillary columns.

The literature is full of such examples and continues to expand at an ever-increasing rate. In addition to the several texts that contain examples of such determinations (3, 81, 82), the reader is referred to several periodicals in which accounts and details of GC assays for drugs (and/or metabolites) in biological fluids are regularly published. These include: *Chromatographia*, *International Journal of Pharmaceutics*, *Journal of Chromatographic Sciences*, *Journal of Chromatography–Biomedical Applications*, *Journal of Pharmaceutical and Biomedical Analysis*, *Journal of Pharmaceutical Sciences*, *Pharmaceutical Research*, *Therapeutic Drug Monitoring*, and LC–GC

FUTURE TRENDS

Although the introduction of HPLC has often been perceived as ultimately replacing GC for use in pharmaceutical analysis, perusal of the current literature and new official compendia clearly indicate that GC is "here to stay." The notion of an imminent demise of GC appears unrealistic in the light of innovations and applications that continue to expand. Other innovative quantitative techniques with potential for use in pharmaceutical analysis are certainly looming on the horizon. In particular is the technique of high voltage capillary zone electrophoresis. These newer methods, coupled with the now wellestablished TLC and HPLC methods, will undoubtedly gain more importance and widespread use in the future. However, all these techniques are unlikely to oust GC, since each have their strengths and weaknesses and together compliment the array of techniques and methods for use in pharmaceutical analysis.

Advances in the manufacture of flexible fused silica WCOT columns will almost certainly extend the applications of GC by virtue of their high-resolution capability, while the advent of sophisticated, computerized detectors forecast the improvement in sensitivity and specificity. The use of chiral stationary phases for the resolution of enantiomers is becoming an increasingly important topic in pharmaceutical analyses. The range and availability of various liquid phases for chiral analysis by GC is bound to make this technique extremely valuable for the assay of pharmaceutical raw materials as well as for use in biological fluids.

Multidimensional and multihyphenated techniques may become increasingly useful, particularly for the analysis of drugs in biological fluids where LC–GC interfacing has a great deal of promise with respect to sample cleanup and preparation time (84,85). GC–MS applications continue to grow in number from the qualitative structural identification point of view, for quantitative analysis that uses SIM (86), and for other quantitative applications of GC (in particular, the increasing use of triple-quad MS/MS spectrometers).

Thus, it is apparent that GC has firmly established itself as a valuable technique for the qualitative and in particular, quantitative determination of drugs. Its application in monitoring impurities, volatile matter, intermediates, and related substances in pharmaceutical raw materials and dosage forms makes it currently the method of choice in this respect. Meanwhile, its increasing use for the quantitative determination of some "hard-to-measure" drugs and metabolites in biological fluids suggest that it is likely to remain an important tool in this arena in the future.

APPENDIX

British Pharmacepoeia (BP) and *European Pharmacopoeia (EP)* Applications of GC for the Assay; Chromatographic Purity; Identification; Presence of Volatile Matter, Intermediates and Related Substances; Organic Volatile Impurities; Determination of Water; Presence of Isomers and Racemate Ratios; Determination of Alcohol and Miscellaneou's Uses of GC in Pharmaceutical Raw Materials and Dosage Forms.

REFERENCES

1. Tswett, M.; Ber. Dtsch. Bot. Ges. **1906**, *24*, 316.
2. Martin, A.J.P.; Synge, R.L.M. A New Form of Chromatogram Employing Two Liquid Phases. 1. A Theory of Chromatography. 2. Application to the Micro-Determination of the Higher Monoamino-Acids in Proteins. Biochem. J. **1941**, *35*, 1358.
3. James, A.T.; Martin, A.J.P. Gas–Liquid Partition Chromatography: The Separation and Micro-Estimation of Volatile Fatty Acids from Formic Acid to Dodecanoic Acid. Biochem. J. **1952**, *50*, 679.
4. Prior, F. Doctoral Thesis, University of Innsbruk: , 1947.

5. Cremer, E.; Prior, F.Z.; Electrochem. **1951**, *55*, 66.
6. Ettre, L.S. Early Evolution of Gas Chromatography and Gas Chromatographic Instrumentation. LC–GC **1990**, *8*, 716.
7. Dimick, K.P. The Emergence of a Commercial Gas Chromatograph. LC–GC **1990**, *8*, 782.
8. McWilliam, I.G.; Dewar, R.D. Flame Ionization Detector for Gas Chromatography. Nature **1958**, *181*, 760.
9. Harley, J.; Nel, W.; Pretorius, V. Flame Ionization Detector for Gas Chromatography. Nature **1958**, *181*, 177.
10. Golay, M.J.E. *Gas Chromatography*; Desty, D.H., Ed.; Butterworths: London, 1958; 36.
11. Perry, J.A. *Introduction to Analytical Gas Chromatography*; Chapter 13 Marcel Dekker, Inc.: New York, 1981.
12. Kovats, E.Z.; Analyt. Chem. **1961**, *181*, 351.
13. Ardrey, R.E.; Moffat, A.C. Gas-liquid Chromatographic Retention Indices of 1318 Substances of Toxicological Interest on SE-30 or OV-1 Stationary Phase. J. Chromatogr. **1981**, *220*; 195.
14. In *Clarke's Isolation and Identification of Drugs*; The Pharmaceutical Press: London, 1986; 193–1112.
15. Leathard, D.A.; Schurlock, B.C. *Identification Techniques in Gas Chromatography*; Wiley: New York, 1970.
16. Leathard, D.A. *Advances in Chromatography*; Giddings, J.C., Grushka, E., Keller, R.A., Cazes, J., Eds.; Marcel Dekker, Inc.: New York, 1975; 13, 265.
17. Finkle, B.; Cherry, E.J.; Taylor, D.M. A GLC Based System for the Detection of Poisons, Drugs and Human Metabolites Encountered in Forensic Toxicology. J. Chromatogr. Sci. **1971**, *9*, 393.
18. *The United States Pharmacopeia*; United States Pharmacopeial Convention, Inc.: Rockville, MD, 1960.
19. The British Pharmacopoeia. The Pharmaceutical Press: London, 1968; 1268.
20. Ahuja, S. *Impurities Evaluation of Pharmaceuticals*; Marcel Dekker, Inc.: New York, 1998.
21. *The United States Pharmacopeia/National Formulary (USP 24-NF 19)*; United States Pharmacopeial Convention Inc.: Rockville, MD, 2000.
22. *The British Pharmacopoeia (1999) incorporating the 3rd edition of the European Pharmacopoeia (1997)*; The Stationery Office: London, 1999.
23. Pollack, G.M. Chromatographic Analysis. In *Encyclopedia of Pharmaceutical Technology*; Swarbrick, J., Boylan, J.C., Eds.; Marcel Dekker, Inc.: New York, 1989; 2, 419.
24. Jönsson, J.A. Chromatographic Theory and Basic Principles. *Chromatographic Science Series*; Jönsson, J.A., Ed.; Marcel Dekker, Inc.: New York, 1987; 38, 27.
25. Van Deemter, J.J.; Zuiderweg, F.J.; Klinkenberg, A. Longitudinal Diffusion and Resistance to Mass Transfer as Causes of Non-Ideality in Chromatography. Chem. Eng. Sci. **1956**, *5*, 271.
26. Souter, R.W. Modern Methods of Pharmaceutical Analysis. Schirmer, R.E., Ed.; CRC Press Inc.: Boca Raton Florida, 1982; III, 5.
27. Giddings, J.C. The Random Downstream Migration of Molecules in Chromatography. J. Chem. Ed. **1958**, *35*, 588.
28. Giddings, J.C. *Dynamics of Chromatography, Principles and Theory*; Marcel Dekker, Inc.: New York, 1965.
29. Kline, B.J.; Soine, W.H. *Pharmaceutical Analysis, Modern Methods*; Munson, J.W., Ed.; Chapter I Marcel Dekker, Inc.: New York, 1981.
30. Perretta, A.T.; Am. Lab. **1976**, *35*, 6.
31. Prescott, B.O.; Wise, H.L. Clean Gases for Gas Chromatography. J. Gas. Chromatogr. **1966**, *4*, 80.
32. *A User's Guide to Chromatography*; Regis Chemical Co.: Morton Grov, IL, 1976; 23.
33. Grant, D.W.; Clarke, A. A Study of the Effects of Instrument Variables on Accuracy and Precision in Gas Chromatography. II. Errors Associated with the Injection of Liquid Samples by Microlitre Syringes. J. Chromatogr. **1974**, *97*, 115.
34. Cramers, C.A.; McNair, H.M. *Chromatography. Part A. Fundamentals and Techniques*; Heftmann, E., Ed.; Journal of Chromatography Library; Elsevier Scientific Publishing Company: Amsterdam, 1983; 22A, A203.
35. Jennings, W. *Gas Chromatography with Glass Capillary Columns*; Academic Press: New York, 1980; 53.
36. Freeman, R.P. *High Resolution Gas Chromatography*; Hewlett Packard: California, 1979; 47.
37. Harris, W.E. Some Aspects of Injection of Large Samples in Gas Chromatography. J. Chromatogr. Sci. **1973**, *11*, 184.
38. Grob, K.; Grob, K., Jr. Isothermal Analysis on Capillary Columns without Stream Splitting: The Role of the Solvent. J. Chromatogr. **1974**, *94*, 53.
39. Schomburg, G.; Diehlmann, R.; Husmann, H.; Weeke, F. New Developments with Glass Capillary Column Production and Sampling Techniques. Chromatographia **1977**, *10*, 580.
40. Grob, K.; Grob, K., Jr. On-Column Injection onto Glass Capillary Columns. J. Chromatogr. **1978**, *151*, 311.
41. Grob, K.; HRC & CC. **1978**, *1*, 263.
42. Galli, M.; Trestianu, S.; Grob, K., Jr. HRC & CC. **1979**, *2*, 366.
43. David, D.J. *Gas Chromatographic Detectors*; Wiley-Interscience: New York, 1974.
44. Adlard, E.R. A Review of Detectors for Gas Chromatography. Part 1: Universal Detectors. Part 2: Selective Detectors. Crit. Rev. Anal. Chem. **1975**, *5*, 1.
45. Grob, R.L., Ed.; *Modern Practice of Gas Chromatography*; John Wiley & Sons: New York, 1985.
46. Clement, R.E.; Onuska, F.I.; Eiceman, G.A.; Hill, H.H., Jr. Gas Chromatography. Anal. Chem. **1990**, *62*, 414R.
47. Both, D. *Chromatographic Analysis of Pharmaceuticals*; Adamovics, J.A., Ed.; Marcel Dekker, Inc.: New York, 1990; 49, 119.
48. Elvidge, D.A.; Proctor, K.A. The Use of Gas Chromatography for Determining Water in Pharmaceutical Preparations. The Analyst **1959**, *84*, 463.
49. Zlatkis, A.; Poole, C. Derivatization Techniques for the Electron-Capture Detector. Anal. Chem. **1980**, *52*, 1002a.
50. Paterson, P. Recent Advances in Thermionic Ionization Detection for Gas Chromatography. J. Chromatogr. Sci. **1986**, *24*, 41.
51. Driscoll, J. Review of Photoionization Detection in Gas Chromatography. J. Chromatogr. Sci. **1985**, *23*, 488.
52. Farwell, S.; Barinaga, C. Sulfur-Selective Detection with the FPD: Current Enigmas, Practical Usage and Future Directions. J. Chromatogr. Sci. **1986**, *24*, 483.
53. Anderson, R.J.; Hall, R.C. *Chromatography*; International Scientific Communications Inc., 1981; 1, 64.

54. Nyarady, S.A.; Barkley, R.M.; Sievers, R.E. Redox Chemiluminescence Detector: Application to Gas Chromatography. Anal. Chem. **1985**, *57*, 2074.
55. Hutte, R.; Sievers, R.; et al. Gas Chromatography Detectors Based on Chemiluminescence. J. Chromatogr. Sci. **1986**, *24*, 499.
56. Andrawes, F.; Ramsey, R. The Helium Ionization Detector. J. Chromatogr. Sci. **1986**, *24*, 513.
57. Grayson, M. The Mass Spectrometer as a Detector for Gas Chromatography. J. Chromatogr. Sci. **1986**, *24*, 529.
58. Biemann, K. The Mass Spectrometer as a Detector in Chromatography. J. Chromatogr. Libr. **1985**, *32*, 43.
59. Evershed, R.P. Analysis of Mixtures by Mass Spectrometry. Part 1. Development and New Applications of Gas Chromatography/Mass Spectrometry. Mass. Spectrom. **1987**, *9*, 196.
60. McMaster, M.; McMaster, L. *GC/MS: A Practical Users' Guide*; Wiley-VCH: New York, 1998.
61. Smith, S.; Adams, G. Chromatographic Performance and Capillary Gas Chromatography: Fourier Transform Infrared Spectroscopy. J. Chromatogr. **1983**, *279*, 1358.
62. Demirgian, J.C. Gas Chromatography: Fourier Transform Infrared Spectroscopy: Mass Spectrometry: A Powerful Tool for Component Identification in Complex Organic Mixtures. Trends Anal. Chem. **1987**, *6*, 58.
63. Cone, E.J. *Pharmaceutical Analysis, Modern Methods*; Munson, J.W., Ed.; Marcel Dekker, Inc.: New York, 1981; 143.
64. Coldwell, R.D.; Porteous, C.E.; Trafford, D.J.H.; Makin, H.L.J. Gas Chromatography-Mass Spectrometry and the Measurement of Vitamin D Metabolites in Human Serum or Plasma. Steroids **1987**, *49*, 155.
65. Supina, W.R. *The Packed Column in Gas Chromatography*; Supelco, Inc., 1974; 106.
66. *Chiraldex Capillary GC Columns: A Guide to Using Cyclodextrin Bonded Phases for Gas Chromatography*; Advanced Separation Technologies, Inc., 1990.
67. Baiulescu, G.E.; Illie, V.A. *Stationary Phases in Gas Chromatography*; Chapter 4 Pergamon Press: Oxford, 1975.
68. Dal Norgare, S.; Juvet, R.S. *Gas-Liquid Chromatography*; Wiley-Interscience: New York, 1962; 63.
69. Martin, A.J.; Bennett, C.E.; Martinez, F.W., Jr. *Gas Chromatography*; Noebels, H.J., Wall, R.F., Brenner, N. Eds.; Academic Press: New York, 1961; 363.
70. Griffiths, J.H.; James, D.H.; Phillips, C.S.G. Section 8. Adsorption and Partition Methods. Gas Chromatography. The Analyst **1952**, *77*, 897.
71. Blau, K.; King, G.S. *Handbook of Derivatives for Chromatography*; Heyden and Sons, 1977.
72. Knapp, D.R. *Handbook of Analytical Derivatization Reactions*; Wiley-Interscience: New York, 1979.
73. Ahuja, S. Derivatization in Gas Chromatography. J. Pharm. Sci. **1976**, *65*, 163.
74. Nicholson, J.D. Derivative Formation in Quantitative Gas-Chromatographic Analysis of Pharmaceuticals. Part II, A Review. The Analyst **1978**, *103*, 193.
75. Bailey, L.C. *Remington's Pharmaceutical Sciences*; Mack Publishing Company, 1985; 17, 603.
76. Barnes, R.L. *Chromatographic Analysis of Pharmaceuticals*; Adamovics, J.A., Ed.; Chapter 6 Marcel Dekker, Inc.: New York, 1990; 49.
77. McClure, G.L. Improved Determination of Organic Volatile Impurities in Pharmaceutical Materials by <USP-467> Using Automated Static Headspace GC/MS. PDA J. Pharm. Sci. Tech. **1999**, *53*, 129.
78. Paul, L. *Personal Communication, Associate Director, General Policies, Nomenclature and Labeling Division*; United States Pharmacopoeia: Rockville, MD, 2000.
79. Hinshaw, J.V. Headspace Sampling. LC-GC **1990**, *8*, 362.
80. Jack, D.B. *Drug Analysis by Gas Chromatography*; Academic Press: New York, 1984.
81. Tsuji, K. *GLC and HPLC Determination of Therapeutic Agents*; Tsuji, K., Morozowich, W., Tsuji, K., Eds.; Marcel Dekker, Inc.: New York, 1979; 9.
82. Adamovics, J.A. Ed.; *Chromatographic Analysis of Pharmaceuticals*; Marcel Dekker, Inc.: New York, 1990; 49, 225.
83. Schirmer, R.E. Ed. *Modern Methods of Pharmaceutical Analysis*; CRC Press Inc.: Boca Raton Florida, 1990; II, 227.
84. Grob, K. On-line Coupled High-Performance Liquid Chromatography: Gas Chromatography. Trends Anal. Chem. **1989**, *8*, 162.
85. Riekkola, M.L. Applications of On-line Coupled Liquid Chromatography: Gas Chromatography. J. Chromatogr. **1989**, *473*, 315.
86. Cone, E.J. *Pharmaceutical Analysis, Modern Methods*; Munson, J.W., Ed.; Chapter 3 Marcel Dekker, Inc.: New York, 1981.